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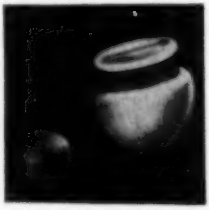

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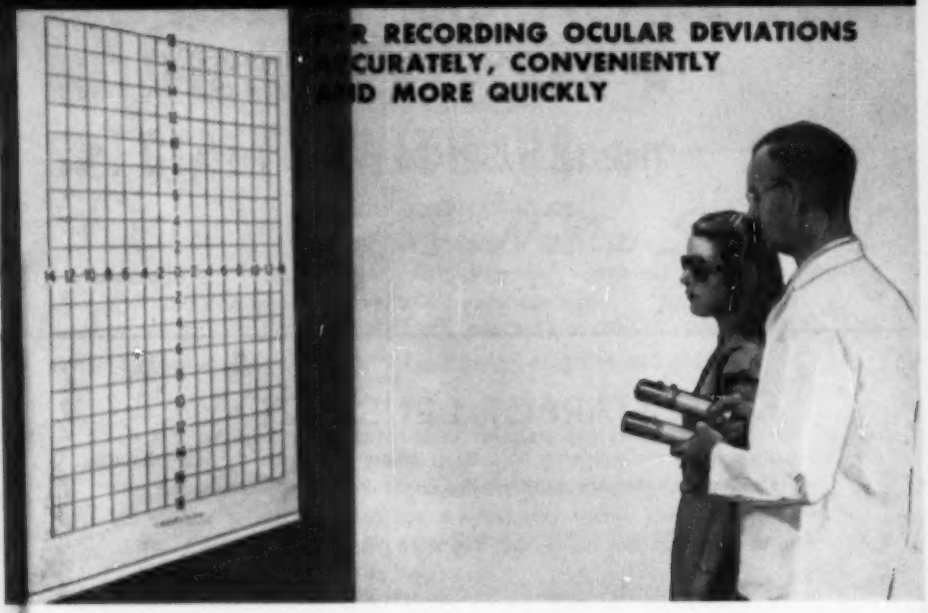

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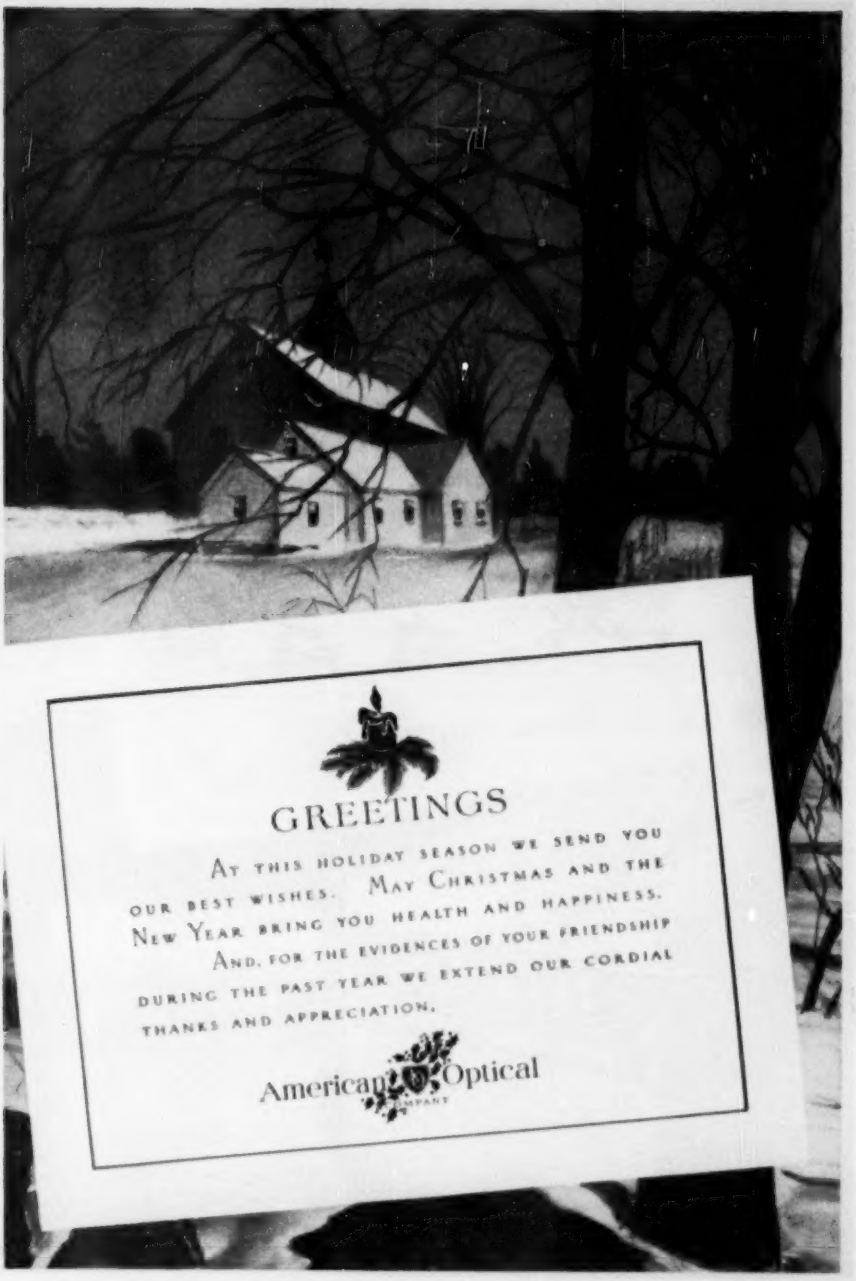
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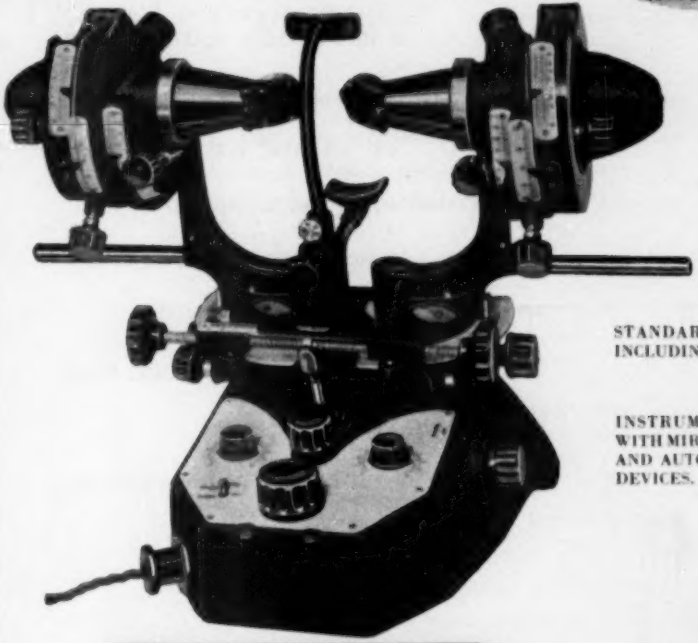

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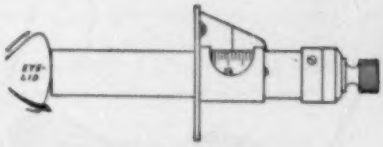

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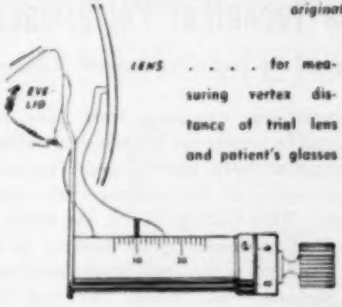

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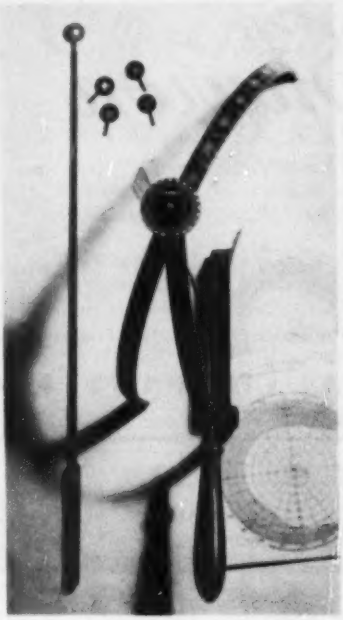

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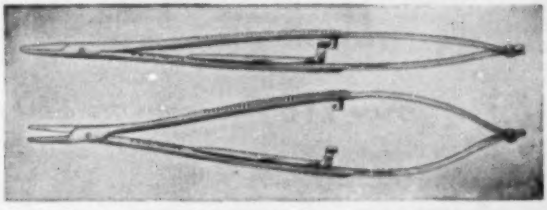

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GONIOPUNCTURE—A NEW FILTERING OPERATION FOR GLAUCOMA

Preliminary Report

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GONIOPUNCTURE is a filtering operation, developed as a result of experiences with goniotomy, which seems of value in juvenile, and possibly congenital, glaucoma. The operation is done by carrying the tip of a knife, devised for this purpose, across the anterior chamber as in goniotomy; but, instead of sweeping the knife along the angle, a counterpuncture into the subconjunctival space is made through the trabecular region of the corneoscleral wall. When the operation is successful, a permanent fistula is established which permits subconjunctival drainage of aqueous humor, indicated by normalization of tension and diffuse edema of the conjunctiva over the area adjacent to the puncture. A persistent hole usually can be seen by gonioscopic examination in the angle wall at the site of the puncture.

Although the data accumulated are as yet insufficient, goniopuncture seems effective in treatment of juvenile glaucoma and may offer promise in congenital glaucoma. It has been ineffective against chronic simple (wide angle) glaucoma. The operation offers several advantages over other types of procedure. The eye operated on retains a normal appearance, the pupil remaining intact. Annoying massive cicatrices do not develop. The procedure is simple, and complications are rare. Convalesence has been rapid.

The operation was developed as a result of observations following goniotomy on the left eye of a 19 year old white girl who had advanced juvenile glaucoma in each eye, manifested by almost complete glaucoma cups, optic nerve atrophy, poor visual acuity and only residual fields. Because miotics were ineffective, the ocular tension remaining at levels of 60 mm. of mercury or more, surgical intervention was considered impera-

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From the Department of Ophthalmology, Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, and Children's Hospital of Philadelphia.

tive. Goniotomy was selected because it had proved to be a safe procedure in treatment of congenital glaucoma, and one which, if unsuccessful, would not interfere with a subsequent filtering operation should further surgical treatment be necessary. Furthermore, its use against juvenile glaucoma, for which there is at least a congenital predisposition, seemed justifiable in view of the excellent results reported in its use in the treatment of congenital glaucoma by Barkan [1] and Scheie.[2] A goniotomy, therefore, was done on the left eye on Jan. 13, 1949, without complication. A minimal postoperative reaction resulted, and the tension was normalized. Gonioscopic examination done one week after operation revealed rather startling results. A gaping cleft, undoubtedly caused by the goniotomy knife, could be seen in the trabecular region along the entire length of the goniotomy incision (fig. 1). Within this cleft, at 8 o'clock, was a darker gray area, which appeared to be a perforation

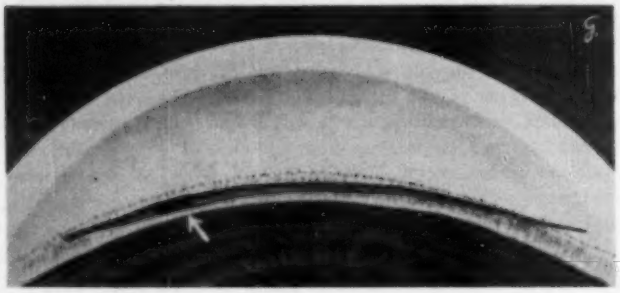

Fig. 1.—Gonioscopic view of angle of left eye, showing cleft in trabecular region; arrow points to fistulous opening.

through the entire thickness of the corneoscleral wall. Subsequent examinations with the slit lamp revealed diffuse edema of the conjunctiva over the nasal half of the globe adjacent to the perforation, presumably due to the subconjunctival drainage of aqueous humor. These two findings seemed sufficient to indicate that goniotomy had controlled the tension in this eye as a result of accidental perforation through the trabecular region with fistula formation.

An attempt then was made to accomplish a similar result in the opposite eye by making only a counterpuncture through the trabecular region with a Barkan knife. No attempt was made to carry out a

1. Barkan, O.: Technic of Goniotomy for Congenital Glaucoma, Tr. Am. Acad. Ophth. **52**:210-226 (Jan.-Feb.) 1948.

2. Scheie, H. G.: Goniotomy in the Treatment of Congenital Glaucoma, Arch. Ophth. **42**:266-282 (Sept.) 1949.

sweeping incision of the angle. The tip of the knife was passed only into the subconjunctival space, not perforating the conjunctiva. After this simple procedure the tension in this eye also remained at a normal level. Diffuse conjunctival edema developed over the segment of the globe surrounding the area of the counterpuncture, and gonioscopic examination revealed an oval, gaping hole at the site of the counterpuncture (fig. 2). The tension in each eye has remained normal during the year and a half since operation, and the diffuse conjunctival edema has persisted unchanged.

Since these initial observations, 16 eyes (11 patients) have been operated on in a similar way. No complications have been encountered. The method failed in all seven eyes (five patients) operated on for chronic simple glaucoma and in one eye operated on for glaucoma

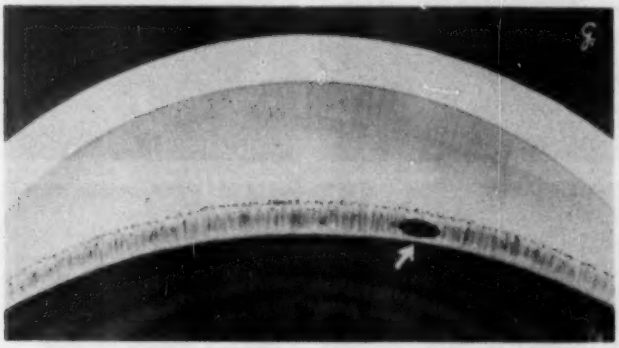

Fig. 2.—Gonioscopic view of angle of right eye, showing gaping hole at site of goniopuncture.

capsulare. All of these patients were over 43 years of age. Four eyes (two patients) were operated on for juvenile glaucoma, and five eyes (four patients), for congenital glaucoma. The tension was controlled in all of the eyes with juvenile glaucoma and in three of the five eyes with congenital glaucoma. Trial and error has resulted in the following rather simple technic, which will undoubtedly be further modified and refined if the operation continues to hold promise.

TECHNIC

The operation is done with the use of local anesthesia, tetracaine being instilled locally, supplemented by the retrobulbar injection of procaine hydrochloride. The O'Brien akinesia is used. Pilocarpine nitrate, 1 per cent, is instilled one hour and one-half hour before operation to prevent mydriasis following the retrobulbar anesthesia. Miosis is desirable during the operation. The contracted pupil protects

the lens and gives less likelihood of the formation of peripheral anterior synechias, which may close the trabecular fistula. To permit prompt restoration of the anterior chamber, a preliminary oblique knife needle puncture, as described by Chandler,[3] is made in the upper temporal quadrant (fig. 3 *A*). Saline solution injected through this opening after completion of the operation promptly restores, and even deepens, the anterior chamber and aids in the prevention of anterior synechias, which could close the fistula. The conjunctiva adjacent to the lower limbus is then ballooned outward away from the globe by the subconjunctival

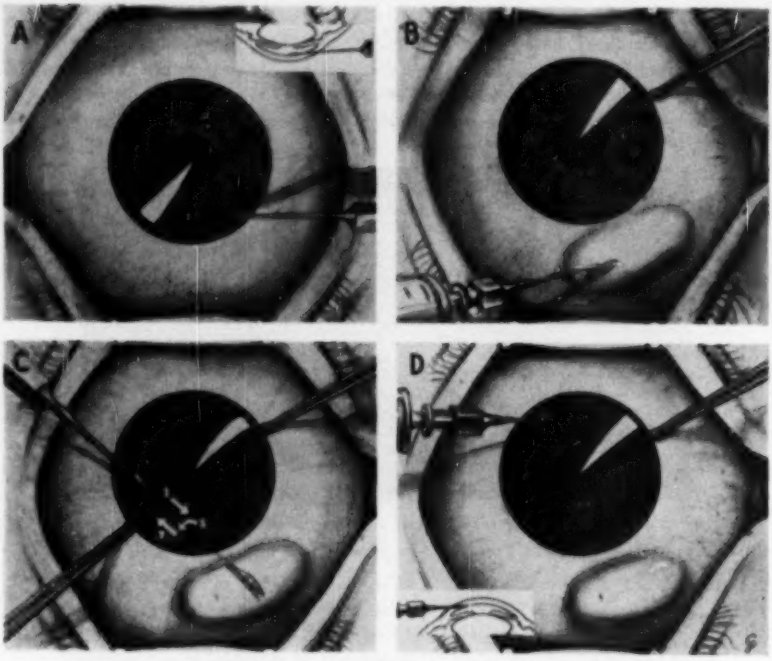

Fig. 3.—*A*, oblique puncture with knife needle to prepare tract for injection of air or saline solution; *B*, raising of conjunctival wheal; *C*, goniopuncture knife: (*1*) puncture and counterpuncture with knife blade in plane of iris; (*2*) knife turned at right angles with cutting edge forward, and (*3*) knife drawn into anterior chamber; *D*, anterior chamber filled with air or saline solution.

injection of saline solution (fig. 3 *B*). This maneuver prevents perforation of the conjunctiva by the knife when one is making the counterpuncture. A knife, specially devised for this operation, is then introduced through clear cornea 1 to 1.5 mm. within the limbus at approximately 9:30 o'clock in the right eye and 2:30

3. Chandler, P. A.: Symposium on Primary Glaucoma: V. Complications of Surgery, Tr. Am. Acad. Ophth. **53**:224-231 (Jan.) 1949.

o'clock in the left eye and directed nasally to the 6 o'clock meridian (fig. 3*C*). The blade is introduced flat, on a plane parallel with the iris, and the tip is carried across the chamber until it reaches the trabecular region of the opposite angle. It is then thrust forward through the corneoscleral wall until the cutting end of the knife is entirely visible beneath the previously ballooned conjunctiva. The knife is then rotated at right angles until it is perpendicular to the iris, the cutting edge being turned forward toward the apex of the cornea. It is then drawn back into the anterior chamber, where it is rotated on its long axis to its original position and withdrawn from the eye. A Barkan knife was originally used, but the proximal edge of the cutting surface was rather sharply angled and blunt, making withdrawal into the chamber hazardous. A new knife was therefore made having a cutting surface with a curvature such that the heel cuts with as much facility as the tip. It has a tapered handle, similar to that of the Barkan knife, and increases in size toward the handle end. This cutting feature is essential in order that an anterior chamber be maintained throughout the operation. Occasionally a small hyphema results, or a small amount of bleeding occurs beneath the conjunctival flap, but as yet this has resulted in no serious difficulty. The anterior chamber is then filled with saline solution injected through a hypodermic needle introduced into the knife needle tract without entering the anterior chamber (fig. 3*D*). Both eyes are covered for only a few hours. Atropine can be instilled 24 hours after operation if the reaction should seem sufficiently severe.

Case 1.—D. E., a white girl aged 19 years, was admitted to the ophthalmology clinic, Hospital of the University of Pennsylvania, on Jan. 6, 1949, because of progressive loss of vision in each eye of about one year's duration. She had had no pain or headache, and no history of seeing halos about lights was elicited. She had had no previous ocular disease. There was no history of familial disease of the eyes. The general physical examination was noncontributory. Routine laboratory studies, including serologic tests, gave normal results.

Ophthalmologic Examination—Vision: Vision was 6/60 in the right eye and 6/60 in the left eye without correction; it was not improved with pinhole disk.

External Examination: External examination revealed no abnormality. Both corneas were clear. The anterior chambers were normal in depth.

Ophthalmoscopic Examination: The media were clear. Almost complete glaucomatous cupping was present in each eye. Each cup was 4 to 5 D. in depth. Optic nerve atrophy was pronounced. Both fundi were otherwise normal except for a rather large, dilated inferior temporal vein in the right eye.

Slit Lamp Examination: No abnormality was found.

Gonioscopic Examination: The angle of each eye was open. The trabecular regions were normal.

Visual Fields: Residual central fields of about 10 degrees in each eye were recorded with 15/1000 and 20/1000 white test objects. These fields were only slightly larger when recorded on the perimeter with a white 10/330 test object.

Ocular Tension: Tension was $0:7.5 = 63$ mm. Hg (Schiøtz) in the right eye and $0:7.5 = 63$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course: A regimen of miotics was started immediately. Pilocarpine did not alter the tension, although the pupils were constricted to 3 mm. Diisopropyl fluorophosphate (DFP) was likewise ineffective, in spite of maximal miosis. Operation was therefore elected, and a goniotomy was done on the left eye on Jan. 13, 1949, for the reasons previously stated. The goniotomy knife was swept along the angle from approximately 11 to 7 o'clock. Little reaction followed, and the tension remained within normal limits. Postoperative gonioscopic

examination revealed a gaping cleft along the entire extent of the goniotomy incision (fig. 1). This was located in the trabecular area of the angle throughout its entire length except at the superior tip at 4 o'clock, which was just anterior to Schwalbe's line. In the neighborhood of 8 o'clock a darker gray area could be seen, which was suspected of being a hole through the entire thickness of the corneoscleral coat. Subsequent slit lamp examination of the conjunctiva over this region confirmed this finding by demonstrating the presence of diffuse conjunctival edema, thought to be due to subconjunctival drainage of aqueous humor. Because the tension in this eye remained normal during the ensuing three weeks, while the tension in the fellow eye continued at an extremely high level, operation was elected for the other eye as well. Assuming that success of the goniotomy could be ascribed to the accidental formation of a subconjunctival fistula, an attempt was made on February 8 to simulate the procedure in the right eye. The anterior chamber was entered with a Barkan knife at 7 o'clock, a simple counterpuncture

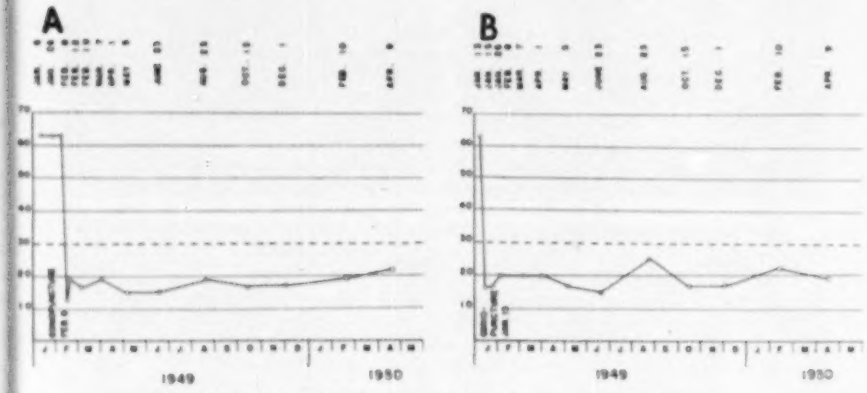

Fig. 4 (case 1).—Ocular tensions (*A*) in right eye and (*B*) in left eye.

was made at 1:30 o'clock, and the knife was made to pass through the recess of the angle into the subconjunctival space. When the knife was withdrawn from the eye, the anterior chamber was filled with air. During the first 36 hours following operation the tension remained elevated, probably owing to the same mechanism which gives a rise in tension after a paracentesis. Subsequently, however, the tension returned to normal and has remained so since. Postoperative gonioscopic study demonstrated an oval hole at the site of the puncture in the angle (fig. 2). Diffuse, persistent conjunctival edema developed over the upper nasal quadrant of the left eye. This eye and its fellow have been followed for nearly a year, and at no time has the tension again become elevated (fig. 4). The last ocular tension was recorded on June 14, 1950 and found to be 20 mm. of mercury (Schiötz) in each eye. The conjunctival edema has continued, and the openings through the trabecular portion of the angles, as seen with a gonioscope, have not changed. Each eye is practically normal in appearance when looked at without magnification. The conjunctival edema is so diffuse and mild that it is easily overlooked.

CASE 2.—K. H., a Negro woman aged 50, was first admitted to the glaucoma clinic of the Hospital of the University of Pennsylvania on Dec. 11, 1947. About one month previously she had noticed that the vision in her left eye was extremely poor. She had then seen her own ophthalmologist, who told her she had glaucoma, prescribed miotics and referred her for further care. No history of pain or of seeing halos around lights could be elicited. She had no family history of serious ocular diseases, including glaucoma. The results of general physical examination were not remarkable. Routine laboratory tests showed nothing abnormal.

Ophthalmologic Examination.—Vision: Vision was 6/6 in the right eye and 6/22 in the left eye without correction; with correction it was 6/5 in the right eye and 6/22 in the left eye.

External Examination: Both pupils were small at the time of initial examination because of miotics which she had been using. The pupillary reactions were therefore of poor amplitude. The anterior chambers were of normal depth. The external condition was otherwise normal.

Ophthalmoscopic Examination.—The media were clear, and both fundi were healthy except for bilateral glaucomatous cupping, much more pronounced on the left. Both optic nerves were atrophic.

Slit Lamp Examination: Both anterior segments were normal.

Gonioscopic Examination: Both angles were wide open. The ciliary portion of each angle could be visualized. A moderate amount of pigment was present in each trabecular zone. No other abnormality existed.

Visual Fields: Determination of the visual fields demonstrated no field defect in the right eye, but the field of the left eye had been reduced to 5 degrees centrally and a small temporal island as recorded with a 10/1000 white test object.

Ocular Tension: The initial tension reading with both pupils constricted to 2.5 mm. was $5 : 7.5 = 30$ mm. Hg (Schiøtz) in the right eye and $4 : 7.5 = 35$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—Miotic therapy was continued with pilocarpine, carbachol, furtrethonium (furmethide®), neostigmine and diisopropyl fluorophosphate being used at different times. The tension was fairly well controlled in each eye until May 1949, when local allergy to furtrethonium developed. Other miotic agents were then employed, but an allergic reaction, even to pilocarpine, ensued. Because she was unable to use miotics, the tension rose to as high as 48 mm. of mercury in the right eye and 55 mm. of mercury in the left eye. She was therefore admitted to the Hospital of the University of Pennsylvania, where a goniopuncture was done on her left eye on June 8, 1949. The operation was performed uneventfully and caused very little reaction. During the evening after the operation the tension was in the neighborhood of 40 mm. of mercury, but by the following morning it was 19 mm. Operation was performed on the right eye on June 13. After operation the tension in the right eye behaved in the same way as had the tension in the left eye. It became elevated during the evening after operation but dropped to a normal level the next day. Postoperative goniscopic examination did not reveal a gaping opening at the site of the goniopuncture in either eye. Instead, only a translucent line containing a small amount of pigment could be seen at the operative site.

Subsequently the tension in each eye gradually rose. That in the left eye was recorded as 35 mm. of mercury on July 1 and gradually climbed to a level of 60 mm. of mercury on November 14. The tension in the right eye remained within normal

limits for a somewhat longer time, staying below 35 mm. of mercury until mid-August. Later it rose to levels of 40 mm. of mercury or above. She was readmitted to the hospital in November, where an iridencleisis was done on the right eye. Miotics were still not tolerated.

CASE 3.—M. J., a white woman aged 29, was referred by Dr. Bourne Jerome, of Minneapolis, because of bilateral juvenile glaucoma. She had been unaware of any ocular difficulty until routine examination in Dr. Jerome's office in May 1949. Her general health was good. There was no family history of ocular disease.

Ophthalmologic Examination.—Vision: Vision was 6/21 in the right eye and 6/30 in the left eye without correction; with correction it was 6/15 in the right eye and 6/9 in the left eye.

External Examination: Both corneas were somewhat large. The interpupillary distance was 70 mm. The pupils were approximately 4 mm. in diameter and reacted poorly as a result of pilocarpine, which she had been using locally.

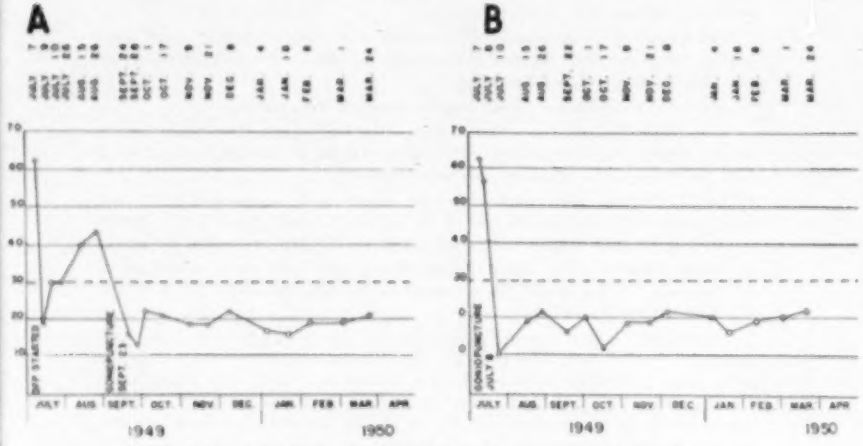

Fig. 5 (case 3).—Ocular tensions (*A*) in right eye and (*B*) in left eye.

Ophthalmoscopic Examination: The media were clear. Rather broad, but incomplete, glaucomatous cups were present in each eye. Definite pallor of each nerve head was seen. The fundi were otherwise healthy.

Slit Lamp Examination: A rather typical picture of posterior embryotoxon with adherence of the anterior layer of the iris to the periphery of the cornea was found.

Gonioscopic Examination: The anterior layer of the iris was adherent to the cornea at the level of Schwalbe's line, which was represented by a hyalin-like band. Numerous defects or fenestrations were seen in the anterior layer of the iris, which permitted free access of aqueous humor to the recess of the angle in each eye.

Visual Fields: A superior nasal defect, typical of glaucomatous change, was found in the left visual field. No defect could be elicited on the right to 1/1000 white or 5/1000 red-green test objects.

Ocular Tension: Tension was 4 : 7.5 = 35 mm. Hg (Schiøtz) in the right eye and 0 : 7.5 = 63 mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—The patient was admitted to the Hospital of the University of Pennsylvania on July 7, 1949, where a goniopuncture was done on the left eye the following day. The fistula was made below at 6 o'clock. A few hours after operation the tension of this eye was 55 mm. of mercury, but the following morning the tension was 40 mm. of mercury and 24 hours after operation it fell to 19 mm. of mercury. Subsequent readings ranged from 15 to 22 mm. of mercury. She was then discharged from the hospital and returned to the care of Dr. Bourne Jerome. Diisopropyl fluorophosphate was prescribed for the other eye, but the tension was only temporarily controlled. A superior nasal defect appeared in the visual field of this eye; so she returned to the hospital for operation on September 22. A goniopuncture was performed on the right eye on September 23. Seven hours after operation the tension was 48 mm. of mercury, but by the following day it had fallen to 17 mm. and since that time has never been above normal limits (fig. 5). Postoperative gonioscopic examination revealed a small oval opening at the site of the goniopuncture in each eye, and diffuse conjunctival edema was seen externally over the site of the punctures with a slit lamp microscope. These findings together with the normalization of tension seemed sufficient evidence that subconjunctival filtration had been established. Dr. Jerome reported her ocular tension to be 17 mm. of mercury (Schiøtz) in the right eye and 24 mm. in the left eye on June 9, 1950.

Case 4.—H. B., a Negro woman aged 55, was admitted to the glaucoma clinic of the Hospital of the University of Pennsylvania on Feb. 3, 1948, where the diagnosis of chronic simple (wide angle) glaucoma of the left eye was established. An adequate history was difficult to obtain, but she stated that she had had blurred vision in the left eye for only three weeks. She had had no pain or discomfort. No halos had been noticed around lights. There was no family history of ocular disease.

Ophthalmologic Examination.—Vision: Without correction, vision was 6/6 in the right eye and was limited to light perception in the left eye.

External Examination: Her pupils showed the typical reaction associated with left optic nerve atrophy. Slight haziness of the left cornea was noticed. The external condition was otherwise normal.

Ophthalmoscopic Examination: Her fundi were healthy except for an almost complete glaucomatous cup in the left eye.

Slit Lamp Examination: Minimal bedewing of the epithelium of the left cornea was present.

Gonioscopic Examination: Both angles were wide open. All angle detail was easily seen. The trabecular region of the left angle was much more pigmented than that of the right.

Visual Fields: The right visual field was normal. Only a residual temporal field for light remained in the left eye.

Ocular Tension: Tension was 5 : 5.5 = 22 mm. Hg (Schiøtz) in the right eye and 0 : 7.5 = 63 mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—Although miotics failed to lower the tension of the left eye, we originally decided not to operate on this nearly blind eye because of the danger of sympathetic ophthalmia. It seemed logical, however, to try goniopuncture, because the uveal tract is not involved in the infiltration procedure. The operation was done on July 8, 1949; but, although no difficulty was encountered,

the tension of the eye was not lowered. The operation was therefore repeated on July 13. After the second procedure, the tension remained in the neighborhood of 30 to 35 mm. of mercury for about a month. It then assumed a somewhat higher level, which was, however, definitely lower than that before operation. Postoperative gonioscopic examination revealed no definite opening; instead, there was a slightly pigmented line at the site of the punctures.

Case 5.—H. C., a Negro woman aged 66, was referred to the glaucoma clinic of the Hospital of the University of Pennsylvania on Sept. 8, 1948, by Dr. Isador Kaplan, with the diagnosis of chronic simple glaucoma. The disease had been discovered while the patient was being treated for conjunctivitis in June 1948. She was receiving miotics at the time she came to the clinic. There was no history of congestive attacks.

Ophthalmologic Examination.—Vision: Vision was limited to light perception in the right eye and was 6/12 without correction and 6/6 with correction in the left eye.

External Examination: No abnormality was found. Pupillary reactions were difficult to elicit because of pronounced miosis due to pilocarpine.

Ophthalmoscopic Examination: Both fundi were normal except for advanced glaucomatous cupping on the right, with nasal displacement of the vessels. Pulsation of the arteries could readily be seen on the right disk.

Slit Lamp Examination: Numerous very fine pigment deposits were present on the posterior corneal surface of each eye.

Gonioscopic Examination: Both angles were open. The trabecular region of each eye showed excessive pigmentation.

Visual Fields: Only a residual temporal field for light remained in the right eye. The left visual field was normal to test objects as small as 1/1000 white.

Ocular Tension: Tension was $2:7.5 = 48$ mm. Hg (Schiøtz) in the right eye and $3:7.5 = 37$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—Miotics of various types were prescribed and used during the ensuing ten months. The tension in the right eye was never controlled adequately, and during June 1949 it showed a definite tendency to become even higher. A goniopuncture was therefore done on July 13, 1949. The operation was accomplished uneventfully, but the tension remained at a level as high as any before operation. Postoperative gonioscopic studies revealed no patent opening at the site of the puncture.

Case 6.—A. C., a Negro woman aged 43, first came to the ophthalmology clinic of the Hospital of the University of Pennsylvania on Oct. 27, 1948, having been referred by the department of cutaneous medicine, where she was undergoing antisyphilitic treatment. She stated that she had noticed blurring of vision for several years. This had not been accompanied with pain or halos about lights.

Ophthalmologic Examination.—Vision: Vision in the right eye was equal to counting fingers eccentrically, and in the left eye it was 6/6 without correction.

External Examination: The right pupil reacted very sluggishly to direct light but constricted promptly to consensual stimulation. No other abnormality was found.

Ophthalmoscopic Examination: The media were clear in both eyes. Nearly complete glaucomatous cupping was present in the right eye, with pronounced optic nerve atrophy. The vessels were displaced nasally. The cup on the right appeared deep and broad, but the color of the nerve head was good. The fundi were otherwise normal.

Slit Lamp Examination: Both anterior segments were normal. The chambers were of good depth.

Gonioscopic Examination: Both angles were open. Excessive pigmentation was not present.

Visual Fields: Only a temporal island of vision remained in the right eye. The left visual field was normal.

Ocular Tension: Tension was $1:7.5 = 55$ mm. Hg (Schiøtz) in the right eye and $2:7.5 = 40$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—This patient was followed in the glaucoma clinic of the hospital, but her ocular tension was never adequately controlled by miotics; readings of 50 mm. of mercury were obtained on frequent occasions. Furthermore, during the nine months she was under observation she was very uncooperative.

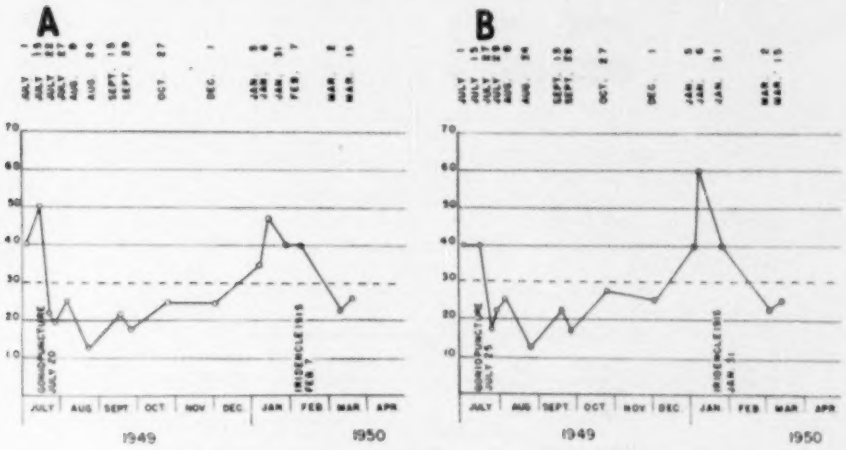

Fig. 6 (case 6).—Ocular tensions (*A*) in right eye and (*B*) in left eye.

For this reason she was admitted to the Hospital of the University of Pennsylvania on July 19, 1949, where a goniopuncture was performed uneventfully on her right eye on the following day. A similar operation was done on her left eye on July 25. Her ocular tension was well controlled without miotics until December 1949, when it again became elevated. An iridencleisis has since been done on each eye, with successful lowering of the tension (fig. 6).

Case 7.—A. O. K., a white boy aged 12 years, was first admitted to the ophthalmology clinic of the Hospital of the University of Pennsylvania on May 20, 1946, because of poor vision in his left eye. This had first been discovered four months before, during a routine examination of his eyes by the school physician. He also had had some discomfort in the eye. No history of previous ocular difficulty could be obtained. He had had measles at 5 years and mumps at 7 years of age. No family history of ocular disease could be elicited. The results of a general physical examination were not remarkable.

Ophthalmologic Examination.—Vision: Vision was 6/9 in the right eye and was limited to perception of hand movements in the left eye, without correction.

External Examination: The eyelids were normal. The left palpebral fissure was slightly wider than the right, and the left eyeball was somewhat more prominent than the right. Both corneas were slightly large, although clear. The left measured 14 mm. in diameter, and was larger than the right (13 mm.). Ocular rotations were full. The conjunctiva and sclera appeared healthy. The pupils were round and regular, but the left (5 mm.) was larger than the right (4 mm.). Both reacted promptly in convergence. The right pupil contracted well to direct light but poorly to indirect light. The left pupil behaved in the opposite manner, a response characteristic of damage to the left optic nerve.

Ophthalmoscopic Examination: The right fundus was normal. The left nerve head was very pale, and a large glaucomatous cup was present, extending to the

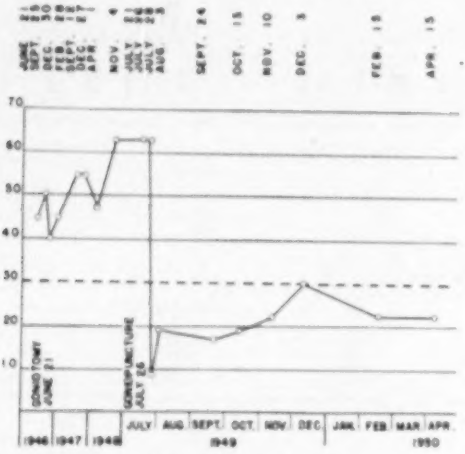

Fig. 7 (case 7).—Ocular tensions in left eye.

margin of the disk. The vessels dropped sharply over the edge. Arterial pulsation was seen at the edge of the cup.

Slit Lamp Examination: The corneas were clear except for rupture of Descemet's membrane in each eye.

Ocular Tension: Tension was 4 : 5.5 = 22 mm. Hg (Schiøtz) in the right eye and 3 : 7.5 = 35 mm. Hg (Schiøtz) in the left eye.

Visual Fields: The right visual field was normal to 1/330 and 1/1000 white test objects. Only a residual temporal field to light remained in the left eye.

Subsequent Clinical Course.—Instillations of pilocarpine nitrate, 1 per cent, and physostigmine salicylate, 0.5 per cent, were prescribed four times daily for the left eye, but this medication failed to reduce the tension, which remained between 36 and 42 mm. of mercury during the following week. Use of diisopropyl fluorophosphate, 0.1 per cent, once daily likewise was ineffective, although extreme miosis resulted. The child was therefore admitted to the hospital, where a goniotomy on the left

eye was performed on June 21. A considerable hyphema occurred, which absorbed promptly. The tension at the time of his discharge from the hospital was 22 mm. of mercury in the surgically treated eye; however, it remained normal for only a short time. By August 5 it was found to be 35 mm. of mercury and subsequently fluctuated between 40 and 65 mm. of mercury (fig. 7). Goniopuncture therefore was performed on July 6, 1949 on the left eye; the counterpuncture was made at the 6 o'clock meridian. The technic of operation was varied slightly. A Ziegler knife needle was used in order to obtain a larger opening than usual in the very wide angle. An incision was made along the plane of the iris for about 4 mm. The knife was then turned forward at a right angle and the incision extended in this direction anteriorly to the point where the conjunctiva joined the cornea. No difficulty was encountered, and the ocular tension has since been normal. However, a rather extensive anterior synechia can be seen at the site of the incision in the angle. The opening still seems to drain adequately, because diffuse conjunctival edema can be seen over the lower portion of the globe adjacent to the site of puncture. The tension, last taken on June 12, 1950, was found to be 22 mm. of mercury (Schiøtz) in the left eye. The tension in the other eye has always been normal; this was apparently a case of spontaneous recovery from congenital glaucoma.

Case 8.—G. C., a white woman aged 57, was first seen on Aug. 2, 1949, because of blurred vision in the right eye. She had never been told that she had glaucoma. She had no other complaints. She stated that she had always been very myopic. There was no family history of ocular disease. Her general health was good. Routine laboratory studies revealed nothing remarkable.

Ophthalmologic Examination.—Vision: Without correction vision was 1/60 in each eye; with correction it was 6/21 in the right eye and 6/12 in the left eye. Correction was -8.75 sph. $\bigcirc -1.00$ cyl., axis 90 for the right eye and -12.75 sph. $\bigcirc -1.50$ cyl., axis 100 for the left eye, with 3.50 D. added.

External Examination: The left pupil was slightly larger than the right, although the right pupil reacted more sluggishly than the left.

Ophthalmoscopic Examination: Both fundi were myopic. Considerable chorioretinal atrophy characteristic of myopia was seen around each disk. There was some fine stippled pigmentation of the right macula. The left macula was normal. The nerve heads did not appear to be cupped excessively.

Slit Lamp Examination: In the right eye definite absorption of the pigment layer of the iris was present at the pupillary border. The lens showed the classic signs of an exfoliating lens capsule. In the left eye, the anterior segment appeared normal except for early changes of senile cataract. The lens capsule in this eye also appeared normal.

Gonioscopic Examination: The angle of the right eye was open. A considerable amount of flaky capsular material was seen over the lower portion of the cornea and the angle of the anterior chamber. Considerable migration of pigment was manifested by a heavily pigmented trabeculum.

In the left eye the angle was open. Neither excessive pigmentation nor capsular material was present.

Visual Fields: A large cut in the inferior nasal visual field was detected in the right eye with a 3/330 white test object. The central field showed considerable constriction above and nasally with the 5/1000 white test object.

The visual field of the left eye was full.

Ocular Tension: Tension was $0:7.5 = 62$ mm. Hg (Schiøtz) in the right eye and $6.5:5.5 = 15$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—Neither 1 nor 4 per cent pilocarpine nitrate was effective in lowering the tension. Diisopropyl fluorophosphate, 0.1 per cent, was then prescribed, to be used daily. This lowered the tension over a period of three days, but the patient complained bitterly of discomfort and blurring of vision. Because of the extreme miosis and incipient changes in the lens, her vision had been reduced to 6/150 in the treated eye. A goniopuncture was done on the right eye on August 10; this controlled the tension for only a short time, and use of pilocarpine had to be started on September 8. The operation must therefore be adjudged a failure.

CASE 9.—L. W., a white girl aged 6 months, was admitted to the Children's Hospital of Philadelphia on Nov. 20, 1949, because of bilateral congenital glaucoma. The diagnosis had been made at another hospital, where bilateral goniotomy had been performed on Nov. 1, 1949. Because the tension had remained elevated in each eye, the patient was referred to the Children's Hospital for further treatment. The mother stated that the child's eyes had been noted to appear enlarged and somewhat cloudy at 2½ months of age. An older brother was blind in both eyes as a result of congenital glaucoma. Except for the ocular condition, the physical examination revealed nothing abnormal. Routine laboratory tests were noncontributory.

Ophthalmologic Examination.—Vision: The patient followed a light with each eye.

External Examination: Both corneas were very hazy. A corneal opacity at the point of entrance of the goniotomy could be seen within the temporal limbus of each eye. The corneal diameter of the right eye was 13 mm., and that of the left eye, 14 mm. The pupils reacted to light.

Ophthalmoscopic Examination: The fundi could not be seen.

Ocular Tension: Tension was $3:7.5 = 41$ mm. Hg (Schiøtz) in the right eye and $1:7.5 = 55$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—Bilateral goniopuncture was done on November 22, with the patient under ether anesthesia. Operation was accomplished uneventfully. However, neither anterior chamber could be filled with air or saline solution, owing to the rapid escape of the injected material through the fistulous opening into the subconjunctival space. Convalescence in the right eye was uneventful. In the left eye, however, leakage from the anterior chamber was so rapid that the chamber could not be formed for three days. Air was injected into the anterior chamber at that time, and the eye quieted rapidly. The right cornea cleared completely except for ruptures in Descemet's membrane, but the left remained hazed, because of permanent scarring. Subsequent tension readings were recorded with the patient under ether anesthesia, on November 29, December 6 and December 20, when the tension was recorded as 25 mm. of mercury in the right eye and 30 to 35 mm. of mercury in the left eye. The patient was subsequently readmitted on Feb. 17, 1950, when the tension, with general anesthesia, was found to be 20 mm. of mercury in the right eye and 35 mm. of mercury in the left eye. At this time a combined goniotomy and goniopuncture was performed on the left eye. A goniotomy incision was made from 11 to 7 o'clock, at which point the knife was carried through the corneoscleral wall to accomplish a goniopuncture as well, thus offering the advantage of both procedures. The tension remained normal in the left eye for only a short time. When last taken, with the patient under anesthesia, on June 9, the tension was 15 mm. of mercury in the right eye and 35 mm. (Schiøtz) in the left eye. This represented a follow-up period of six months.

CASE 10.—B. L., a white girl aged 9 years, was first admitted to the Children's Hospital of Philadelphia on Jan. 30, 1950, because of glaucoma in the left eye. The child had had some pain and discomfort in this eye at times since the age of 4 years. The diagnosis of glaucoma had been made by a local ophthalmologist in October 1949, and the child had then been referred for further care. Her general health was good. There was no family history of glaucoma. The general physical examination was noncontributory. Routine laboratory studies revealed nothing abnormal.

Ophthalmologic Examination.—Vision: Vision was 6/9 + in the right eye and 6/150 in the left eye without correction and 6/6 — in the right eye and 6/20 in the left eye with correction.

External Examination: A slight ptosis of the left eyelid was noted. The right cornea measured 11.5 and the left 12.5 mm. in diameter. The left eyeball seemed definitely larger than the right. The right pupil measured 3.5 mm. and the left 5 mm. in diameter. The pupillary reactions were normal on the right and were definitely sluggish on the left. Both corneas were clear.

Ophthalmoscopic Examination: The right fundus was healthy. The left showed excavation of the nerve head, typical of glaucoma. The central arteries pulsated strongly. No other abnormality was found.

Slit Lamp Examination: The anterior segment of each eye was normal. No rupture of Descemet's membrane was seen.

Gonioscopic Examination: The angles were open in each eye. No abnormality was found.

Visual Fields: The right visual field was normal. The left showed localized nasal contraction with general depression of the central fields to 1/330 and 1/1000 white test objects.

Ocular Tension: Tension was 5 : 5.5 = 20 mm. Hg (Schiøtz) in the right eye and 2 : 7.5 = 46 mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—A goniopuncture was done on Jan. 31, 1950, with the patient under general anesthesia. Operation was uneventful. The anterior chamber was easily filled with air. Convalescence was marred by a rather severe hemorrhage in the anterior chamber, which occurred on the third day but absorbed during the next four or five days. The eye quieted promptly. The child was followed for 10 days after operation, when, probably owing to increased protein in the aqueous humor, the tension had not returned to normal. At this time the patient left the city, to be under the care of another ophthalmologist. The tension was subsequently reported to us on two occasions as being 30 mm. of mercury (Schiøtz), the last determination being made on April 27 by Dr. Herbert Levitt, of Toronto, Canada.

CASE 11.—S. G., a white boy aged 5 months, was admitted to the Children's Hospital of Philadelphia because of unilateral congenital glaucoma. At 2 months of age the right eye was noticed to be larger than the left and the cornea steamy in appearance. A diagnosis of congenital glaucoma was made by his local ophthalmologist, who treated him with miotics. Because they failed to control the tension of his left eye, the child was referred for further care. His general health was good. There was no family history of ocular disease. The general physical examination was noncontributory. Routine laboratory studies likewise revealed nothing abnormal.

Ophthalmologic Examination.—Vision: The child followed objects with each eye.

External Examination: The right cornea was steamy in appearance; the left was clear. The diameter of the right cornea was 14 mm. and that of the left 12 mm. The right pupil was slightly larger than the left and reacted sluggishly; the left pupil reacted promptly.

Ophthalmoscopic Examination: The fundus in the right eye could not be seen; the fundus in the left eye was normal.

Slit Lamp Examination: A horizontal tear was present in Descemet's membrane of the right cornea. Epithelial bedewing was present, as well as some hazing of the stroma. The anterior segment of the left eye was normal.

Gonioscopic Examination: The right eye was too hazy to permit visualization. In the left eye the angle was open. No abnormality was found.

Ocular Tension: Tension was $2:7.5 = 46$ mm. Hg (Schiøtz) in the right eye and $5:7.5 = 30$ mm. Hg (Schiøtz) in the left eye.

Subsequent Clinical Course.—A goniopuncture was done on the right eye on Jan. 6, 1950. Operation was performed without difficulty, although the chamber could not be filled with air after operation, the air escaping into the subconjunctival space through the goniopuncture opening. Convalescence was uneventful. The child was reexamined under general anesthesia on January 12, at which time the tension was 20 mm. of mercury (Schiøtz) in each eye. Ophthalmoscopic examination revealed definite glaucomatous cupping on the right. Gonioscopic examination revealed the angle to be open throughout except temporally at 9 o'clock, where an anterior synechia had formed at the site of the goniopuncture through the cornea. The cornea remained clear, but, when examined with the patient under vinyl ether (vinethene®) anesthesia on April 28, the tension of the right eye was found to be 42 mm. of mercury. A combined goniotomy and goniopuncture was then done, as described in case 10.

COMMENT

Goniopuncture has been used for the treatment of 16 eyes with glaucoma. Six had chronic simple (wide angle) glaucoma, one had glaucoma capsulare, four had juvenile glaucoma and five had congenital glaucoma. All of the eyes were characterized by having open angles. The operation failed in six eyes with chronic simple glaucoma and one eye with glaucoma capsulare, but it successfully controlled the tension in all four of the eyes with juvenile glaucoma and in three of the five eyes with congenital glaucoma (table). The eyes operated on for juvenile glaucoma have been observed for periods of from nine months to nearly a year and a half following the procedure. Those operated on for congenital glaucoma have been followed for only six months, which is too short a time for final evaluation, particularly since the tension of both eyes of one patient operated on for chronic simple glaucoma remained normal for six months after operation before again becoming elevated.

There can be little doubt that goniopuncture lowers the ocular tension as a result of the formation of a fistulous opening through the corneoscleral wall, through which aqueous drains subconjunctivally. Such a mechanism is indicated by the presence of a persistent hole at the site of the puncture, which can be seen gonioscopically, and by diffuse edema of the conjunctiva overlying the region of the puncture.

Because these phenomena associated with goniopuncture were first observed in an eye after goniotomy, interest in the mechanism of action of goniotomy immediately was aroused. The way in which goniotomy acts has been the subject of considerable debate since its use was first advocated by Tailor [4] (1891) and de Vincentiis [5] (1893). These two workers believed that goniotomy was effective through incision of the tissue of the iris angle, which resulted in débridement of the angle of the anterior chamber. De Wecker, on the other hand, disagreed and engaged in a long controversy with de Vincentiis after an article [6] (1895) in which he discussed de Vincentiis' procedure. In his opinion, the operation lowered ocular tension by incision of the internal layers of the sclera,

Results of Goniopuncture

Case No.	Eye	Type of Glaucoma	Stage of Disease	Age	Date of Operation	Result *
1	OD	Juvenile	Advanced	19 yr.	2/ 8/49	+
	OS	Juvenile	Advanced	.....	1/13/49	+
2	OD	Chronic simple	Early	50 yr.	6/13/49	—
	OS	Chronic simple	Advanced	.....	6/ 8/49	—
3	OD	Juvenile	Early	29 yr.	9/23/49	+
	OS	Juvenile	Early	.....	7/ 8/49	+
4	OS	Chronic simple	Advanced	55 yr.	7/ 8/49	—
5	OD	Chronic simple	Advanced	66 yr.	7/13/49	—
6	OD	Chronic simple	Advanced	43 yr.	7/20/49	—
	OS	Chronic simple	Early	.....	7/25/49	—
7	OS	Congenital	Advanced	15 yr.	7/30/49	+
8	OD	Glaucoma capsulare	Moderately advanced	57 yr.	8/10/49	—
9	OD	Congenital	Moderately advanced	5 mo.	11/21/49	+
	OS	Congenital	Moderately advanced	.....	11/21/49	—
10	OS	Congenital	Advanced	9 yr.	1/31/50	+
11	OD	Congenital	Moderately advanced	6 mo.	1/12/50	—

* A successful result is indicated by +; a failure, by —.

thus providing access of the aqueous to the lymph spaces of the angle of the anterior chamber, and by furnishing more direct contact with the venous sinuses of the angle. He even noted the possibility of escape of aqueous into the episcleral and conjunctival vessels, but did not mention having made a perforating incision. This difference of opinion has never been resolved, although nowadays most workers favor the hypothesis that goniotomy strips embryonic tissue away from the wall of the angle of the anterior chamber, thus permitting access of the aqueous to the canal of Schlemm. The observations reported here which led to gonio-

4. Tailor, U.: Sulla incisione dell'angolo irideo (contributione alla cura del glaucoma), Ann. di ottal. **20**:117-127, 1891-1892.

5. de Vincentiis, C.: Incisione dell'angolo irideo nel glaucoma, Ann. di ottal. **22**:540-542, 1893.

6. de Wecker, L.: Sclerotomie luterme, Ann. d'ocul. **114**: 103-117, 1895.

puncture indicate, however, that the sclerotomy, with subsequent subconjunctival filtration, does occur as a result of goniotomy in at least some instances. I therefore reexamined all of the eyes with congenital glaucoma previously treated by goniotomy.[2] No evidence of a cleft or filtration could be found in any eye.

No mention of an operation identical to goniopuncture has been found in the literature. The procedure involves the principles of anterior sclerotomy; its only new aspect is incision from inside the anterior chamber. Valude and Duclos[7] (1898) mentioned perforation of the sclera as one of the possible complications of goniotomy but carried the thought no further. Bader[8] (1876) described an operation employing somewhat the same principles in which a subconjunctival limbal section was made with a Graefe knife superiorly over one third of the circumference of the limbus. The knife entered and left the anterior chamber beneath the conjunctiva and was carried upward until the corneoscleral tissues had been divided. A conjunctival bridge, as wide as possible, was preserved. Filtration occurred beneath this bridge. Staphyloma formation, however, was not infrequent, and the operation never gained widespread use.

Goniopuncture seems to offer promise in the surgical treatment of juvenile and congenital glaucoma. It has been easy to perform. No serious complications were encountered in the series of operations here reported. An occasional hemorrhage in the anterior chamber complicates the procedure, but absorption has always been prompt.

A secondary rise in tension, which persists for several hours, sometimes occurs. This is probably comparable to the secondary rise in the tension which follows paracentesis, for the goniopuncture opening is very small and it is probably incapable of compensating for the increased flow of fluid associated with plasmoid aqueous formation but is sufficient to care for ordinary needs.

The goniopuncture opening should not be too large because of the danger of anterior synechia, with obstruction of the fistula. A large opening would become sealed, for the same reason that the iris comes forward to obstruct a corneoscleral trephine opening if no iridectomy has been done. It is possible that a technic for goniopuncture may be evolved in which an iridectomy can be done. The operation might then be useful in the treatment of chronic simple (wide angle) glaucoma, in which apparently a larger opening is necessary than in the glaucoma occurring in younger age groups.

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7. Valude and Duclos: Du débridement de l'angle iridien, Ann. d'ocul. **119**:98-116, 241-272, 1898.

8. Bader, C.: Sclerotomy Versus Iridectomy, Ophth. Hosp. Rep. **8**:430-433, 1876.

The period of convalescence is short. One eye is uncovered only a few hours after operation, and the patient is then allowed out of bed. The eye retains a normal appearance after the surgical procedure. There are no annoying scars or colobomas. The filtration area is diffuse, and no bulging cicatrix of the conjunctiva occurs. The conjunctival edema caused by the filtration is so slight that slit lamp magnification is usually necessary to be sure of its presence.

Goniopuncture eliminates the necessity of dissection of a conjunctival flap and thus avoids trauma to Tenon's capsule and the episclera, which necessarily occurs with other types of filtering operations, such as the corneoscleral trephine and iridencleisis. Such trauma leads to scarring and sealing of the trephine opening, with failure in control of ocular tension. Goniopuncture, by creating a direct opening into the epibulbar space beneath Tenon's capsule, avoids this hazard. That the communication is existent can be proved by the marked ballooning of the conjunctiva and Tenon's capsule as aqueous escapes through the fistula immediately after goniopuncture or, as occasionally occurs, when the anterior chamber is reformed with air or saline solution.

Reasons for success or failure of the operation are obscure. The factor which seems of most importance is that of age. Goniopuncture has failed permanently to control the ocular tension of any eye when the patient was over 29 years of age but has been successful in a high percentage of patients below this age. Postoperative gonioscopic examination suggests that the explanation might be some fundamental change in ocular tissues which occurs with advancing age. In younger patients, after successful goniopuncture, a gaping hole can be seen in the trabecular region at the site of the puncture wound. This resembles a trephine opening and shows no subsequent tendency to close. In the eyes of older patients, the tissues at the site of the puncture do not gape but, instead, coaptate, falling into their original positions. It seems possible that the corneoscleral tissues of younger persons are sufficiently elastic to permit the cut edges to retract, causing gaping of the wound, whereas in older people the tissues are more rigid and inelastic. As a result, prompt coaptation takes place, and the wound later closes.

The stage of the glaucoma seems of little importance in influencing the outcome of the operation. The first patient with juvenile glaucoma, both of whose eyes were successfully operated on by goniopuncture, had nearly complete glaucoma cups with lowered visual acuity and residual visual fields; yet the operation was successful in each instance. This was also true in two of the eyes operated on for congenital glaucoma in which the disease was far advanced prior to surgical intervention. In one of these eyes a previous goniotomy had failed to lower the ocular tension.

The value of goniopuncture cannot be truly assessed at the time of writing. The number of eyes operated on by this method is too small to warrant final conclusions, and the follow-up period, particularly for the eyes operated on for congenital glaucoma, likewise has been much too short. Suffice it to say that the operation has controlled the tension of the four eyes operated on for juvenile glaucoma, all of which have been followed for from nine months to 1¼ years and of three to five eyes with congenital glaucoma, although followed for no longer than six months. Goniotomy, done three years previously, had failed to control the tension of one of these eyes with congenital glaucoma.

Goniopuncture is now being tried on a series of eyes with congenital glaucoma in combination with goniotomy to utilize the advantages of each procedure. The usual goniotomy incision is made, at the lower extremity of which the knife is thrust through the corneoscleral wall to reach the subconjunctival space. Regardless of the ultimate value of goniopuncture, conclusive evidence is offered that goniotomy, at least occasionally, can be effective through the formation of a fistula.

CONCLUSIONS

1. Goniopuncture is a filtering operation developed as a result of observations following goniotomy.

2. The operation consists in making a fistula through the trabecular region of the corneoscleral wall by an incision from inside the anterior chamber, resulting in subconjunctival drainage of aqueous humor.

3. The operation offers promise in the surgical treatment of juvenile and congenital glaucoma.

4. Goniopuncture offers an explanation for the mechanism of action of goniotomy in at least certain instances.

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ABSTRACT OF DISCUSSION

DR. A. EDWARD MAUMENEE, San Francisco: Dr. Scheie is to be congratulated on benefiting from his operative mistake in puncturing the sclera when he was attempting to do a goniotomy. This demonstrates the value of careful clinical examination of patients. If more of us were as careful in our observations, we should know more about congenital glaucoma today. Dr. Scheie's operative procedure was excellently described, and it sounds as though it would be—technically—easy.

The main value of this paper is that it gives further insight into the mechanism of action in angle operation for congenital glaucoma. My colleagues and I have recently examined 12 children under the age of 1 year with normal eyes to see whether there was evidence of mesodermal tissue in the angle of the anterior chamber. The angles appeared very similar to the angles of many children with congenital glaucoma; that is, the iris inserted onto the sclera rather than the ciliary body, and in most instances there was a fine meshwork of tissue on the corneoscleral

trabeculae which is not seen in adult eyes. In none of the normal eyes did the iris adhere to Schwalbe's line, as it does in an occasional patient with congenital glaucoma. If these observations are valid, it is unlikely that goniotomy functions in cases of congenital glaucoma by removing mesodermal tissue from the angle, as has been suggested recently.

Dr. Scheie has demonstrated by his successful operations that there is a fundamental difference in the chamber angle of children and of adults with glaucoma. It is not known whether this is due to the position of Schlemm's canal, the vascular plexus in the sclera, the elasticity of the tissues or some other factor.

Does Dr. Scheie think there is any difference in the mode of action of his operation and that of the Herbert limbal puncture? What is the basis for the diagnosis of juvenile glaucoma? Is there an anatomic difference in the eyes with juvenile and arrested congenital glaucoma and those with adult glaucoma?

DR. WILLIAM J. FERGUSON, San Francisco: No one type of surgical procedure controls all forms of congenital glaucoma. Most common surgical procedures, useful for adult glaucoma, have had poor success with congenital glaucoma. When goniotomy fails, a dilemma arises. What then offers relative safety and a fair incidence of success? Few procedures offer both. Dr. Scheie's success with this filtering type of operation demonstrates a relatively safe procedure which has had good results in his hands.

For the past two years, I have been associated with Dr. Otto Barkan. During that time we have operated on 30 children with congenital glaucoma, or 53 eyes. Congenital glaucoma is a serious disorder. Some of the affected children have eyes already badly damaged at birth by high intraocular pressure. Some have associated serious developmental defects. Some are neglected and brought to the ophthalmologist with badly stretched and damaged eyes.

In case 7 of Dr. Scheie's series, the eye with a cornea 14 mm. in diameter is a badly stretched eye. We are reluctant to do a goniotomy on such an eye. The incidence of serious hemorrhage is high, and that of success is low. I hope Dr. Scheie's procedure will continue to prove useful in cases of this type.

An occasional accident in doing a goniotomy operation is perforation of the sclera subconjunctivally. A bleb of aqueous quickly forms. We have watched filtration through some fistulas for two weeks. All such fistulas in our series have spontaneously closed. This is shown by gonioscopic examination and lack of subconjunctival edema or bleb formation.

Years ago, during the development of his goniotomy, Dr. Barkan did a small series of operations in which he closely followed the technics of DeWecker. The cornea was punctured, the knife was passed across the chamber, and a counterpuncture was made in the sclera of the opposite chamber angle. The knife was then withdrawn slightly, and stripping of the chamber angle was done. Success in this group was less than in those in which no counterpuncture was done, and the procedure was dropped. External filtration was temporary only.

Dr. Scheie suggests that the mode of action of the goniotomy is external filtration. The following observations are evidence against this: 1. Bleb formation or subconjunctival edema is not seen. 2. In only a small group has perforation of the sclera occurred. 3. Microgonioscopy

shows no fistulous openings in the wall of the chamber angle. 4. There is a high degree of correlation between the postoperative tension and the degree and extent of cleaning or stripping of the chamber angle, as seen by microgonioscopy.

Dr. Harold G. Scheie, Philadelphia: I wish to thank Dr. Maumenee and Dr. Ferguson for discussing this paper. Dr. Maumenee has compared this procedure to Herbert's operation. The mechanism is undoubtedly the same, although the approach is different. There is less trauma to the subconjunctival tissue with goniopuncture. Furthermore, there seems more certainty of passing the knife through the trabecular portion of the angle with goniopuncture than with Herbert's procedure.

Dr. Maumenee also asks for a definition of juvenile glaucoma. This is difficult, except on an age basis. Glaucoma occurring in patients younger than 30 years of age is arbitrarily classified as juvenile glaucoma unless the patient is so young that the ocular tissues undergo enlargement as a result of increased intraocular tension. Then the disease is called congenital, or infantile, glaucoma. Occasionally abnormal tissue can be seen in the angles of eyes with infantile and juvenile glaucoma, but in the greater number of cases no abnormality is found, even though one must assume a congenital predisposition. Since there is no fundamental difference in the behavior or appearance of eyes with juvenile and those with chronic simple glaucoma, the differentiation must be made on age alone.

The fact that Dr. Barkan has experimented with a procedure similar to goniopuncture is not surprising in view of his pioneer work in glaucoma. His work was apparently done on infants, in whom I have found the results to be less encouraging with goniopuncture than in the age group with juvenile glaucoma. The explanation is uncertain, although one reason may be that the anterior chamber in infants reforms with difficulty. The fistula becomes obstructed, owing to anterior synechia. Instead of remaining in the anterior chamber, air or saline solution promptly pushes out through the fistula and into the subconjunctival space, tending to produce collapse of the globe and anterior chamber. The answer may be a combination of goniopuncture and iridotomy. In several cases I have tried incising the corneoscleral wall at the completion of a sweeping goniotomy incision, the procedure which Dr. Ferguson has just said Barkan has done. I cannot accept Dr. Ferguson's flat statement that he is sure the goniopuncture fistula closes. The edema of the conjunctiva is extremely filmy and can easily be missed unless one is on guard.

UNILATERAL INTERNUCLEAR OPHTHALMOPLEGIA

Report of Eight Clinical Cases with One Postmortem Study

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AND
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BOSTON

PARALYSIS of both medial rectus muscles on attempted conjugate lateral gaze without other evidence of third nerve paralysis is an entity known as internuclear ophthalmoplegia. It is relatively common and almost invariably due to multiple sclerosis. Paralysis of one medial rectus muscle on attempted conjugate lateral gaze is much less common. It is the purpose of this communication to present eight cases of the unilateral syndrome and to describe the anatomic lesions in one. The latter is the first case of unilateral internuclear ophthalmoplegia in which a pathologic study has been carried out. In only a single case of the bilateral syndrome has postmortem examination been made.[1]

Internuclear ophthalmoplegia is presumed to result from a lesion of the medial longitudinal fasciculus with consequent interruption of the impulses from a center in the medulla on one side to the medial rectus nucleus on the opposite side. The syndrome has been produced experimentally in animals by lesions of the medial longitudinal fasciculus,[2] and stimulation experiments have shed some light on the course of the fibers in the brain stem,[2b] although the actual site of crossover of the fibers has not been clearly demonstrated. The hypothetical site of such a lesion in man has been represented diagrammatically.[3] The clinical manifestations of inter-

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1. Spiller, W. G.: Ophthalmoplegia Internuclearis Anterior: A Case with Necropsy, Brain **47**:345, 1924.

2. (*a*) Klossowsky, B., and Levikowa, A. M.: Der Mechanismus der vestibularen Nystagmus. (Über die homonyme keineswegs cruciate Innervation der Musculi recti interni von dem Oculomotoriuskern beim Nystagmus), Arch. f. d. ges. Physiol. **228**:198, 1931. (*b*) Bender, M. B., and Weinstein, E. A.: Effects of Stimulation and Lesion of Median Longitudinal Fasciculus in the Monkey, Arch. Neurol. & Psychiat. **52**:106 (Aug.) 1944.

3. Cogan, D. G.: Neurology of the Ocular Muscles, Springfield, Charles C Thomas, Publisher, 1948.

nuclear ophthalmoplegia consist of paralysis of the medial rectus muscle on attempted conjugate lateral gaze. As a rule there is preservation of medial rectus function on convergence. Horizontal, rotary or vertical nystagmus is frequently present, and it is characteristic for the horizontal nystagmus to be much more marked in the abducting eye. A vertical divergence of the eyes (skew deviation) is also often present. The onset of internuclear ophthalmoplegia is frequently accompanied with vertigo and sometimes with nausea and vomiting.

Cases of unilateral internuclear ophthalmoplegia previously recorded total something less than 10. The data given in some of these reports are too meager to permit a clearcut differentiation between the unilateral and the asymmetric bilateral syndrome. The following eight cases appear to have been instances of unilateral internuclear ophthalmoplegia. Sauvineau [4] reported a case in a patient with syphilis; the symptoms lasted one month and had the unusual feature of being associated with homolateral ptosis. Fischer [5] reported a case in which the patient had a widespread neurologic disorder of undetermined etiology. Jaensch [6] reported a case of paresis of the medial rectus, following trauma, that was associated with unilateral superior oblique and sympathetic paralysis. This case, and possibly others in which the data given are inadequate to permit judgment, were incorporated in a subsequent report [7] on internuclear ophthalmoplegia. Lutz [8] reported one case in which he thought the ophthalmoplegia was due to occlusion of small vessels in the pons and another [9] in which it was associated with postinfluenzal psychiatric disturbances. His first case was noteworthy in that the condition persisted unchanged for several years and was associated with unilateral absence of the blink reflex, and his second had the unusual feature of associated bilateral ptosis. In a case reported by Dunphy [10] the condition came on spontaneously in a man aged 33 after a strenuous game of basketball. His case, like the second in the present series, had the peculiar feature

4. Sauvineau: Un nouveau type de paralysie associée des mouvements horizontaux des yeux, Bull. et mém. Soc. franç. d'opht. **13**:524, 1895.

5. Fischer, O.: Isolierte Lähmung eines Musculus rectus internus als Seitenwender, Prag. med. Wchnschr. **30**:677, 1905.

6. Jaensch, P. A.: Einseitige supranukleare Medialisparese, Klin. Monatsbl. f. Augenh. **73**:471, 1924.

7. Jaensch, P. A.: Zur Klinik der supranuclearen Medialisparese und internuclearen Ophthalmoplegie, Arch. f. Ophth. **125**:592, 1930-1931.

8. Lutz, A.: Über einseitige Ophthalmoplegia internuclearis anterior. (Beschreibung eines neuen Falles in Verbindung mit heterolateraler Herabsetzung des automatischen Blinzelreflexes und Verlust der Reaktionsfähigkeit der homolateralen vertikalen Bogengänge), Arch. f. Ophth. **115**:695, 1924-1925.

9. Lutz, A.: Nachtrag zu meiner Arbeit: Über einseitige Ophthalmoplegia internuclearis anterior, Arch. f. Ophth. **116**:376, 1925-1926.

10. Dunphy, E. B.: Ophthalmoplegia Internuclearis: Report of a Case, Arch. Ophth. **55**:54 (Jan.) 1926.

of severe pain in the face on the side opposite the ophthalmoplegia. Müller and Mani [11] briefly reported two cases of transient nature believed to be due to multiple sclerosis.

REPORT OF CASES

CASE 1.—*Sudden onset of unilateral internuclear ophthalmoplegia, nystagmus and skew deviation in a patient with chronic lupus erythematosus. Small infarct destroying the homolateral medial longitudinal fasciculus near the level of the sixth nerve nucleus revealed at necropsy.*

A. C. (no. 603960), an Italian woman aged 25, was admitted to the Massachusetts General Hospital for the fourth time with an exacerbation of lupus erythematosus. The disease had made its first appearance one year previously as a rash of the face and upper part of the chest, malaise and fever. Shortly afterward, the finger tips became red and tender, and an eruption appeared on the legs. Except for congenital deafness, the patient had previously been well.

Six months after the onset the patient was hospitalized for the first time. Routine examination of the eyes showed nothing abnormal. The rash was maculopapular, and on the face it had a characteristic butterfly distribution. There were also generalized lymphadenopathy and enlargement of the spleen. The Hinton

Fig. 1 (case 1).—Photographs taken from moving picture roll.

(*A*) With gaze directed straight ahead, the left eye was slightly higher than the right, but both eyes were in approximately the primary position of gaze.

(*B*) On looking to the left, the elevation of the left eye was still evident, but there was full adduction of the right eye.

(*C*) On looking to the right, however, there were a lag of the left eye and consequent exotropia.

test of the blood gave a negative reaction. Pneumonia developed, but this was successfully treated with penicillin and the patient was discharged from the hospital.

Ten months after the onset of her illness she had ulcerations in the mouth, further extension of the eruption over the limbs, chills and fever, increased swelling and tenderness of the interphalangeal joints and, later, pleuritic pain. She was readmitted three times for exacerbation of these symptoms.

While in the hospital the fourth, and last, time, she had sudden onset of diplopia. Examination disclosed inability to adduct the left eye on attempted conjugate gaze to the right but normal adduction on convergence. There was skew deviation of approximately 5 degrees, with the left eye higher than the right; this appeared to be the same in all fields of gaze but could not be measured accurately. There were slight vertical nystagmus on looking up and some horizontal nystagmus on looking to either side. On right lateral gaze the nystagmus was more pronounced in the right eye. In contrast to the abnormalities in the left eye, all movements of the right eye were normal (fig. 1).

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11. Müller, H. K., and Mani, P.: Über die isolierte, einseitige, supranukleare Medialislähmung, Klin. Monatsbl. f. Augenh. **97**:685, 1936.

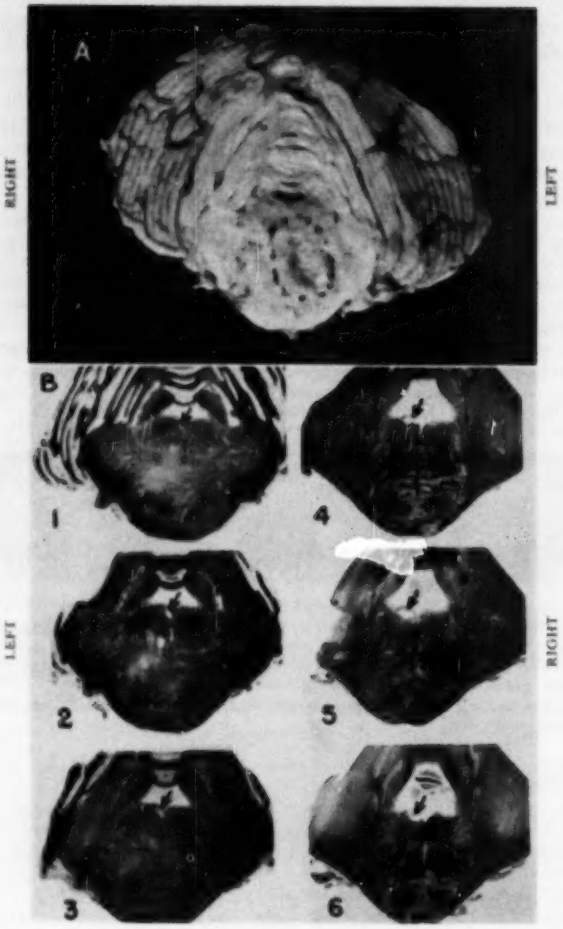

Fig. 2 (case 1).—*A*, section through the pons showing the large infarct on the left side, circumscribed by the dotted line. The smaller infarct, which involved the left medial longitudinal fasciculus, was not evident in the gross specimen.

B, sections of the pons at various levels of the small infarct (indicated by arrows) in the region of the left medial longitudinal fasciculus. The three upper sections also include the larger infarct. Sections are numbered from above downward. Loyez stain for myelin.

There was no obvious paresis of the face, arms or legs; the plantar reflexes were normal, and no other abnormal neurological signs were elicited. The examination was limited, however, because of the patient's deafness and profound illness.

Considerable improvement in the ocular condition occurred, and by the sixth day after the onset of diplopia the left eye was adducted 15 to 20 degrees on attempted right lateral gaze.

Ascites and pulmonary edema developed; the temperature rose to 105 F., and the patient became comatose and died, twelve days after the onset of diplopia and approximately one year after the onset of lupus erythematosus.

Fig. 3 (case 1).—Area from the infarct indicated by arrow in the first section of figure *2 B* and the surrounding region, including the smaller infarct lateral to the right medial longitudinal fasciculus. Cresyl violet stain.

Pathologic Report (autopsy no. 13273).—There were pulmonary congestion and edema and a large serofibrinous pericardial effusion. Microscopic examination disclosed "fibrinoid" necrosis, typical of lupus erythematosus, of the endocardium and serous surfaces and of some of the blood vessels.

The blood vessels, meninges and outer surfaces of the brain and brain stem were grossly normal. Section through the middle portion of the pons at the level of the trigeminal nerves disclosed an oblong, grayish pink, soft area measuring approximately 1 by 0.5 cm., apparently an infarct, situated on the left side, near the midline, at the junction of the base and the tegmentum (fig. *2 A*).

Microscopic Study.—Serial sections of the midbrain and pons were stained by the Loyez method for myelin and with cresyl violet and hematoxylin and eosin (figs. *2 B* and 3). They disclosed (1) recent infarction corresponding

to the region of softening observed at autopsy; (2) a smaller region of infarction, also on the left side, just above the level of the nucleus of the sixth nerve, corresponding very nearly to the position of the medial longitudinal fasciculus, and (3) a very small lesion of similar nature lateral to the right medial longitudinal fasciculus. The larger lesion on the left side measured approximately 1 by 0.5 cm. in its vertical and transverse diameters and an estimated 1 cm. in its longitudinal axis. It was situated near the midline, chiefly in the tegmentum and stratum profundum, and involved the nucleus reticularis tegmenti, the corpus trapezoideum, the lemniscus medialis and only a few fibers of the corticospinal tract. It was rostral to the nuclei and fibers of the sixth and seventh cranial nerves and medial to the nucleus and fibers of the fifth nerve and did not involve any of these structures. The smaller lesion on the left side measured 2.6 and 1.7 mm., respectively, in its greatest transverse and dorsoventral diameters and approximately 3 mm. in length, extending upward from a point slightly rostral to the knee of the facial nerve (through approximately 200 serial sections, 15 microns in thickness) to the upper fibers of the trigeminal nerve. At the level which it occupied it destroyed the greater part of the medial longitudinal fasciculus and some of the dorsal longitudinal fasciculus of Schütz. It did not involve the nucleus or fibers of the sixth nerve.

On the opposite (right) side, in nearly the same position but slightly lateral to the medial longitudinal fasciculus, there was a similar, much smaller lesion, measuring 0.4 mm. in diameter.

The histological appearance of all the lesions was typical of infarction. There was destruction of nerve cells and nerve fibers with characteristic glial and vascular reactions, i. e., numerous microglial phagocytes, pleomorphic microglia cells, pronounced intimal proliferation and, adjacent to the region of necrosis, plump astrocytes. The changes observed were consistent with the 12 day duration of symptoms.

At the inner margin of the lesion of the left medial longitudinal fasciculus was an artery, 0.1 mm. in diameter, filled with an organized thrombus. Many other small blood vessels in the region of the lesion and elsewhere in the brain stem and cerebellum were abnormal. The vascular changes consisted of patchy, adventitial infiltration with lymphocytes and plasma cells and degeneration of the vessel wall, the degeneration often occurring where there was little or no cellular infiltration. Associated with these changes were intimal and adventitial proliferation and sometimes thrombosis. Both arteries and veins were affected. The involvement was patchy, affecting small areas, while the vessels in most parts of the brain were not definitely abnormal.

Comment.—This case provided an unusual opportunity for obtaining evidence as to the localization of lesions responsible for unilateral internuclear ophthalmoplegia. The findings are consistent with the assumption that the isolated paralysis of the medial rectus muscle on attempted conjugate gaze was due to the lesion of the medial longitudinal fasciculus on the side of the affected eye. The vertical and horizontal nystagmus was similar to that occurring with lesions in various regions of the brain stem or cerebellum and could not be specifically attributed to the lesion of the medial longitudinal fasciculus. It was possibly due to involvement of some part of the vestibular complex

CASE 2.—*Sudden onset of vertigo, vomiting, internuclear ophthalmoplegia on the right side, nystagmus, skew deviation and pain over the left eye in a patient with long-standing diabetes. Subsequent appearance of hemorrhagic glaucoma.*

I. O'B. (no. 449134), an Irish housewife aged 62, was admitted to the hospital because of vertigo, pain over the left eye and diplopia, of three days' duration. She had been known to have diabetes, under irregular control, for 13 years. The onset of the present symptoms had been sudden, while she was leaning over an ice box. Immediately after the onset there were vomiting and severe vertigo.

Examination disclosed complete absence of adduction of the right eye on attempted conjugate gaze but normal adduction on convergence. There was approximately a 5 degree deviation of the right eye upward without apparent weakness of any of the vertically acting muscles. Vertical nystagmus was present in the primary position of gaze and was increased on looking upward. Horizontal

Fig. 4 (case 2).—Photographs taken from moving picture roll.

(*A*) With gaze directed straight ahead, the right eye was elevated and slightly divergent.

(*B*) On looking to the right, the right eye was still elevated, but there was full adduction of the left eye.

(*C*) On looking to the left there were apparent complete paralysis of the right medial rectus muscle and slight elevation of the right eye.

(*D*) On convergence, however, there was full function of the right medial rectus muscle.

nystagmus occurred in both eyes on looking to either side, but on looking to the left it was much greater in the left eye, i. e., it was a predominantly unilateral nystagmus. The function of the left medial rectus was normal (fig. 4).

The neurologic status was otherwise normal. The cerebrospinal fluid, including the reaction to the Wassermann test, was normal. The Hinton test of the blood gave a normal reaction.

Two months after the onset there was some improvement in the ophthalmoplegia, but acute glaucoma had developed in the right eye, in which vision was reduced to light perception. The fundus could not be seen; the glaucoma (tension, 60 to

80 mm.) did not respond to miotics, and occlusion of the central retinal vein was suspected. A retrobulbar injection of alcohol was given for the pain, and the patient has not been followed further.

Comment.—The symptoms in this case were similar to those in the preceding one and were probably due also to a vascular lesion (infarct) involving the medial longitudinal fasciculus and vestibular nucleus. Unexplained is the pain in the eye on the side opposite the affected medial rectus muscle and presumably opposite the lesion. It is noteworthy that Dunphy's patient also had severe pain in the face on the side opposite the paralyzed medial rectus muscle.

CASE 3.—*Several transient episodes of diplopia, followed by persistent unilateral internuclear ophthalmoplegia, skew deviation and nystagmus, accompanied with transient numbness of the upper lip on the side of the ophthalmoplegia and with numbness of the hand on the opposite side, occurring in a patient with auricular fibrillation.*

C. L. (no. 660894), an Englishman aged 69, came to the eye clinic on account of diplopia. He had been well until one year previously, when he began having transient episodes of diplopia. Each of these lasted only a few seconds, until six weeks

Fig. 5 (case 3).—(*A*) With the gaze directed straight ahead, there were elevation of the right eye approximately 10 degrees and slight divergence.

(*B*) On looking to the left, the right eye was still elevated approximately the same amount, but there was full adduction of the right eye.

(*C*) On looking to the right, however, there were apparent paresis of the left medial rectus muscle and elevation of the right eye.

before admission, when the patient suddenly experienced persistent diplopia, reeling gait and numbness of the left side of the upper lip and the right hand. The sensory symptoms subsided in a few hours. On his admission to a nearby hospital complete paralysis of the left medial rectus muscle and, allegedly, partial paralysis of the left superior and left inferior rectus muscles were noted. No ptosis or anisocoria was present. There were also some dysarthria, possible weakness of the facial muscles on the right, incoordination of the left upper extremity, intention tremor, more pronounced on the left, and bilateral extensor plantar reflexes. A presumptive diagnosis of infarction of the pons was made. The patient also had auricular fibrillation, thought to be due to arteriosclerotic heart disease, and was digitalized.

On his admission to the eye clinic six weeks later, the left eye could not be adducted more than 10 degrees. On looking to the right, there was horizontal nystagmus, limited to the right eye. Both eyes moved normally to the left. Hypotropia was present in the left eye and increased progressively on looking to the left, attaining a maximum of about 20 degrees, thus simulating paresis of the right superior oblique muscle. There was, however, no gross limitation of movement of this eye. On looking down, there was vertical nystagmus, greater in the left eye. Convergence could not be elicited (fig. 5).

The neurologic status was otherwise normal. The Hinton test of the blood gave a negative reaction, and the spinal fluid was normal.

Sixteen weeks after the onset the findings had not changed.

Comment.—In addition to the unilateral internuclear ophthalmoplegia, skew deviation and nystagmus, there were indications of involvement of the brain stem in the form of crossed sensory symptoms, dysarthria and bilateral extensor plantar reflexes. There were no other indications of third nerve paralysis. The initial impression that there was weakness of the superior and inferior rectus muscles was probably based on a misinterpretation of the skew deviation, since the latter was not mentioned. It is noteworthy that skew deviation simulating paresis of the superior oblique muscle has been reported previously in connection with internuclear ophthalmoplegia (Jaensch,[6] Spiller [1]).

CASE 4.—*Sudden onset of internuclear ophthalmoplegia, skew deviation and nystagmus in a patient with auricular fibrillation.*

T. R. (no. 531173), an architect aged 70, was admitted to the hospital because of diplopia. Two days previously he awoke "seeing double" and noted illusory move-

Fig. 6 (case 4).—(*A*) With gaze directed straight ahead, the right eye was slightly elevated and divergent.

(*B*) On looking to the right, the elevation of the right eye was maintained, and there was full adduction of the left eye.

(*C*) On looking to the left, however, there was apparently complete paralysis of the right medial rectus muscle.

ment of the environment. He had had coronary heart disease and auricular fibrillation for some time.

Examination disclosed complete absence of adduction of the right eye on attempted gaze to the left, but normal convergence. Adduction of the left eye on gaze to the right was normal. In the primary position there was skew deviation, the right eye deviating upward 5 to 10 degrees (fig. 6). This did not change appreciably on looking up or down. There were spontaneous rotary and occasionally vertical nystagmus.

A complete neurologic examination was not performed. The blood pressure was 165 systolic and 100 diastolic.

Comment.—The ocular signs were similar to those in the preceding cases and presumably were due to a small infarct involving the right medial longitudinal fasciculus and vestibular nucleus.

CASE 5.—*Sudden onset of vertigo, vomiting, illusory movement of the environment, internuclear ophthalmoplegia on the right side and nystagmus in a patient with unexplained exophthalmos of the left eye.*

B. S. (no. 34295), a Jewish woman aged 50, came to the eye clinic because of double vision and vertigo, of four days' duration. These symptoms began in the middle of the night as the patient got up to go to the bathroom and were accompanied with nausea, vomiting and an illusory whirling of the room. The vertigo at the onset was so severe that the patient was forced to keep her head immobile. All the symptoms except the diplopia had improved in the four days since the onset.

There was exophthalmos of the left eye, about which the patient volunteered no complaint. On direct questioning she said it had been present for several days but could give no further information about it.

Examination disclosed the following condition: Visual acuity with her own glasses was 20/30 in the right eye and 20/70 in the left eye. There were exophthalmos (right eye, 15 mm.; left eye, 20 mm.) and marked reduction in orbital resiliency of the left eye. On attempted conjugate gaze to the left the right eye moved only a few degrees past the midline, while the left eye abducted normally (fig. 7). In this position there was a coarse nystagmus in the left eye but none in the right. The right eye also lagged behind the left on moving from right to left. On conjugate gaze to the right, there was full excursion of both eyes without diplopia but with horizontal nystagmus, which was slightly coarser in the right eye than in the left. On conjugate gaze downward there was rotary nystagmus of both eyes. On attempted convergence, adduction of the right eye was not any

Fig. 7 (case 5).—Photographs taken from moving picture roll.

(*A*) Position of eyes with gaze directed straight ahead. The eyes are approximately in the primary position.

(*B*) On looking to the right there is full excursion of both eyes.

(*C*) On looking to the left, the right eye goes only a few degrees beyond the midline.

greater than on attempted conjugate gaze. There was questionable lag of the left eye on looking up. The pupils were normal. The disk margins in the left eye were blurred, and there were moderate hypertensive and arteriosclerotic changes in both eyes. The visual fields were normal. The blood pressure was 180/90.

It was thought that there were two unrelated lesions, one of the right medial longitudinal fasciculus and another in the left orbit.

The patient was admitted to the hospital for study. Neurologic examination revealed no abnormality except for the ocular findings. Studies of the spinal fluid showed normal dynamics, a normal protein content and a negative Wassermann reaction. Roentgenograms of the skull, orbit, sinuses and chest showed a normal condition.

Within a few months after the onset, adduction of the right eye returned to normal, but upward gaze of the exophthalmic (left) eye became more limited. The patient has now been followed for six years. There have been occasional attacks of vertigo but no substantial change in the ocular condition. The cause of the exophthalmos is still not apparent. A pneumoencephalogram and an arteriogram showed no abnormality. The basal metabolic rate was normal.

Comment.—The unilateral medial rectus paralysis together with vertigo and an asymmetric nystagmus on attempted lateral conjugate gaze was similar to the symptom complex in the other cases. The lesion was presumably a small infarct. The persistent, and probably unrelated, exophthalmos of the opposite eye is still unexplained.

CASE 6.—*Unilateral internuclear ophthalmoplegia, nystagmus and skew deviation in a child following an infection of the respiratory tract and an episode of vomiting.*

D. S. (no. 689888), a boy aged 5 years, was brought to the eye clinic because of a divergence of the right eye. Two weeks previously he had had a cold, characterized by rhinorrhea and cough but not sufficiently severe to keep him from school. One week later he vomited intermittently for one day and felt ill but did not complain of vertigo, headache or stiff neck; nor was there unusual drowsiness. The temperature was not taken. The following day divergence of the right eye was

Fig. 8 (case 6).—(*A*) With gaze directed straight ahead, the right eye shows right hyperexotropia.

(*B*) On looking to the right, both eyes showed full movement, but the hypertropia was maintained.

(*C*) On looking to the left, the right eye showed limited adduction, but the left eye had full excursions.

(*D*) On looking at a near object, however, there was good convergence, even when the object was placed in the left field.

noted. The patient did not complain of diplopia but did have some difficulty in seeing his coloring book and later developed head turning. The mother thought that some improvement had occurred by the time of admission.

The visual acuity was 20/15 in each eye. In the primary position of gaze the right eye was turned outward about 10 degrees and upward about 5 degrees. On attempted conjugate gaze to the left the right eye was adducted only 20 degrees but on convergence was adducted to a full 45 degrees. On conjugate gaze to the right the excursions of both eyes were normal (fig. 8). There was no limitation of vertical movements of either eye, and the hypertropia of the right eye was approximately the same in all fields of gaze. In the primary position there was conspicuous rotary nystagmus which was converted into vertical nystagmus or

looking upward and a vertical-horizontal nystagmus on looking to either side. The nystagmus was coarser in the left eye on both upward and lateral gaze. The asymmetry was especially evident on looking to the left.

Except for the condition of the eyes, there were no other neurologic abnormalities.

Comment.—In this case, the ocular motor signs were similar to those in the other cases; but, unlike the latter, there was no reason to suspect vascular disease and the pathogenesis was not apparent.

CASE 7.—*Unilateral internuclear ophthalmoplegia and skew deviation in a child associated with transitory unsteadiness of gait and unusual somnolence, possibly related to an infection of the upper respiratory tract.*

R. W. (no. 694742), a boy aged 6 years, was brought to the eye clinic because of dissociation of eye movements. The informant (the grandmother) stated that four days previously the patient had had an earache and cold, followed the next day by marked unsteadiness of gait. He was unusually drowsy and slept most of the day. On the third day, that is, the day prior to his admission to the clinic, there was some puffiness of the lids, and the right eye was noted to deviate outward.

Examination of the eyes revealed complete failure of adduction of the right eye on attempted conjugate gaze to the left and on attempted convergence, and a

Fig. 9 (case 7).—(*A*) On looking to the left, there was normal abduction of the left eye but practically complete absence of adduction of the right eye.

(*B*) On looking straight ahead, the right eye was deviated approximately 20 degrees outward and 5 degrees upward.

(*C*) On looking to the right, there was full movement of both eyes.

skew deviation with the right eye elevated approximately 5 degrees in all fields of gaze. All other ocular movements were normal (fig. 9). The visual acuity was 20/30 + in each eye.

Physical examination, including a neurologic survey, revealed no other abnormality. The spinal fluid pressure was 150 mm. of water; the cell count was 14 lymphocytes per cubic millimeter; the sugar measured 75 mg., and protein 16 mg., per 100 cc.

The patient was observed in the hospital for ten days, during which time the adduction of the right eye improved slightly. On one occasion there was a transient earache, similar to that which he had had at the onset. This was attributed by an otolaryngologist to blockage of the eustachian tube. There were roentgenologic evidence of bilateral sinusitis and increased density of the left mastoid. The rectal temperature did not exceed 100.5 F. at any time.

Comment.—At first glance, the obvious diagnosis was paralysis of one medial rectus muscle, conceivably due to a lesion involving the nerve to the affected muscle. That, however, would not explain the skew

deviation. That the lesion was probably located in the brain stem is further indicated by symptoms and findings suggestive of encephalitis, e. g., somnolence and lymphocytosis in the cerebrospinal fluid.

It is possible that most cases of the condition diagnosed as isolated medial rectus paralysis are actually instances of unilateral internuclear ophthalmoplegia. In view of the intimate association between the representation of the medial rectus and that of the other rectus muscles in the nucleus and trunk of the third nerve, it seems unlikely that any marked disturbance of function of the medial rectus could occur as the result of a lesion of the nucleus or nerve without involvement of other muscles. With this in mind, the files of one of us were reviewed, and the following case was found in which the diagnosis of isolated paralysis of the medial rectus muscle had been made but which in retrospect was probably an instance of unilateral internuclear ophthalmoplegia.

CASE 8.—*Isolated paralysis of the right medial rectus muscle in a patient with long-standing diabetes.*

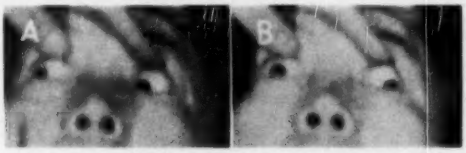

Fig. 10 (case 8).—Photographs taken from moving picture roll.
(*A*) On looking to the right, there was full movement of both eyes.
(*B*) On looking to the left, the right eye could not be adducted beyond the midline.

E. B. (no. 300882), a widow aged 60, had onset of diplopia one week after the incision of a chalazion of the right upper lid. She was known to have had diabetes for approximately twenty years and recently had been on a restricted diet. The patient had been depressed of late.

Examination disclosed that the right eye could not be adducted on attempted conjugate gaze or convergence. All other ocular movements were normal (fig. 10). The pupils were normal. There was extensive diabetic retinopathy. Except for the ocular condition and a blood pressure of 205/110, there were no other abnormal clinical findings.

The patient was not seen until six months later, when she was admitted to the hospital in a highly confused state. The ocular movements were thought to be normal, but lack of cooperation did not permit adequate examination. The patient was discharged to a psychiatric hospital with a diagnosis of vascular disease of the brain and died soon afterward. There was no necropsy.

Comment.—This patient was seen several years ago by one of us, and the case was listed in the files as one of "isolated paralysis of one medial rectus muscle." Routine pictures were taken at that time. The case was recognized as a probable instance of unilateral internuclear ophthalmoplegia only in retrospect.

COMMENT

Internuclear ophthalmoplegia, when it occurs with multiple sclerosis, inflammation or neoplasm, is characteristically bilateral.

Of the foregoing cases of the unilateral syndrome, postmortem examination disclosed a vascular lesion as a cause of the symptoms in one. Judging from the sudden onset and associated vascular disease in most of the other cases, and in the cases previously reported, it seems likely that a vascular lesion is usually responsible for the unilateral syndrome.

Considering the close proximity of the paired tracts of the medial longitudinal fasciculus to each other, the unilateral involvement is of some interest. It is evidently accounted for by anatomic features of the blood supply, in particular by its strict lateralization,[12] because of which an infarct may be limited to one side. The lesion may also be very small, as was illustrated by the postmorten findings in case 1. With lesions such as those of multiple sclerosis, which are not related to the blood supply or bounded by the midline, both tracts are usually involved.

That there are exceptions to the rule is indicated by cases 6 and 7, in which there was no clinical evidence for vascular disease, and by Spiller's case of the bilateral syndrome due to infarction.

SUMMARY AND CONCLUSIONS

Eight cases of the symptom complex known as unilateral internuclear ophthalmoplegia are reported. In every case the onset was sudden, and there was unilateral paralysis of one medial rectus muscle on attempted lateral conjugate gaze. Convergence was normal in four cases and could not be elicited in four. Nystagmus was present in six cases, and skew deviation in six cases. Postmortem examination in one case, of lupus erythematosus, revealed a small region of infarction involving the medial longitudinal fasciculus on the side of the ophthalmoplegia. The pathologic changes in that case and the sudden onset of symptoms and associated vascular disease in most of the other cases were evidence that vascular lesions were generally responsible for unilateral internuclear ophthalmoplegia.

It is suggested that, whereas multiple sclerosis is the chief cause of bilateral internuclear ophthalmoplegia, vascular disease (infarction) is the usual cause of unilateral internuclear ophthalmoplegia.

12. Kubik, C., and Adams, R. D.: Occlusion of the Basilar Artery—Clinical and Pathological Study, Brain **69**:73, 1946, figs. 5 (lower right illustration), 21 and 22 (B and C).

OCULAR THERAPEUTIC PRINCIPLES AND PRACTICAL APPLICATIONS

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AMONG the various drugs used in the treatment of disease during the past 15 years, four principal groups stand out as revolutionary: the sulfonamides, the antibiotics, the antihistaminics and the recently developed steroids of the adrenal cortex and their activating hormones from the anterior lobe of the pituitary gland. It will be my endeavor to review what is known about the mechanism of action of these drugs and to point out practical applications in the field of ocular therapeutics.

The use of the sulfonamides and the antibiotics to attack pathogenic organisms may seem to be a relatively modern procedure, but actually the principles of chemotherapy are not new. Paul Ehrlich,[1] of Germany, formulated them as far back as 1913. He defined chemotherapy as the treatment of parasitic disease by direct chemical attack on the responsible organism with a minimum of damage to the tissues of the host. He showed that certain drugs combined chemically with certain parasites more effectively than they did with the host tissues. He pointed out that this predominant affinity for the parasite might depend on some slight alteration in the chemical structure of the drug. These concepts of Ehrlich opened the way to the discovery of compounds inhibitory to pathogenic organisms and the modification of their chemical structures so that their toxicity to the host might be reduced without impairing their bacteriostatic effect.

THE SULFONAMIDES

Before the introduction of the sulfonamides, in 1935, a number of antiseptic compounds were used in ophthalmology, particularly those employed in an attempt to sterilize the conjunctival sac. The rationale

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1. Ehrlich, P.: Chemotherapeutics: Scientific Principles, Methods, and Results, Lancet **2**:45, 1913.

of their use was that they killed organisms in vitro in a concentration which could be tolerated by the ocular tissues. It was shown, however, that in vivo most of them either combined chemically with conjunctival secretions or interfered with the natural immunologic properties of the conjunctiva, such as lysozyme production and phagocytosis of bacteria, and thus their full effect was greatly nullified.

The advent of the sulfonamides introduced a new era in the science of therapeutics. Although they now have been largely supplanted by the newer antibiotics, they are still useful at times and more of their mode of action is understood. This has been found to depend on their antagonism for paraaminobenzoic acid.[2] Paraaminobenzoic acid is one of the constituents of folic acid, which many bacteria require for their growth.[3] Sulfonamides prevent the utilization of paraaminobenzoic acid into the folic acid molecule. Their effectivity depends on their concentration. The latter must be high enough to overcome the paraaminobenzoic acid present. Organisms which do not require folic acid for their growth are not sensitive to sulfonamides.

In the local use of sulfonamides the following points must be kept in mind:

1. Their effectivity is definitely impeded by the presence of pus and other secretions containing large amounts of paraaminobenzoic acid. Therefore irrigation of the conjunctival sac should be employed before instillation. Also, unless high concentrations are used, they will be ineffective, and high concentrations, in most instances, are obtainable only by employing the sodium salts whose p_H may be so high that irritation of ocular tissues results. A notable exception is sulfacetimide sodium, which has a p_H of 8 and which can be used in 30 per cent solution without irritation. This drug can be successfully employed in cases of conjunctivitis and corneal ulcers caused by sulfonamide-sensitive organisms. It is also useful after minor injuries to the eyes, extraction of foreign bodies, etc., as a prophylaxis against infection. At the Massachusetts Eye and Ear Infirmary my colleagues and I instil 1 drop routinely in every eye after tonometric examination. I venture to predict that this drug may some day be employed as prophylaxis against ophthalmia neonatorum instead of silver nitrate if state laws so permit. Cases of sensitivity must be rare. I have never had an instance during several years' use of this drug, although I have heard of it occurring with others.

2. Regeneration of corneal epithelium is retarded by the sulfonamides. This is less noticeable with drops than with ointment preparations. For

2. Woods, D. D.: Relation of *p*-Aminobenzoic Acid to Mechanism of Action of Sulphanilamide, Brit. J. Exper. Path. **21**:74, 1940.

3. Angier, R. B., and others: Structure and Synthesis of Liver L. Casei Factor, Science **103**:667, 1946.

this reason, it is not wise to use these drugs after extensive corneal abrasions, particularly in ointment form. Swan [4] has pointed out that tiny globules of any ointment may get under the epithelium in any abrasion and delay healing mechanically.

The penetration of the cornea by the various sulfonamides has been studied by Bellows [5] and others. Sodium sulfacetimide appears to possess the best power of penetrating the intact corneal epithelium. Greater penetration can be obtained by combining the drug with a detergent or by employing iontophoresis or a corneal bath. This is rarely necessary, for when the cornea is infected its permeability is altered and all sulfonamides pass through easily.

When given systemically, the sulfonamides diffuse readily into all ocular tissues. It should be the aim of the ophthalmologist to establish and maintain an effective drug level of about 5 to 8 mg. per 100 cc. until all organisms are eradicated. Several factors enter into the maintenance of such a level: (1) the size of the dose, (2) the rate of absorption, (3) the percentage bound to plasma proteins and (4) the rate of excretion. In many ways sulfamerazine is the ideal sulfonamide. It is rapidly absorbed and slowly excreted (chart 1). However, it has the theoretical disadvantage that 84 per cent of it is bound to plasma proteins and hence is ineffective.[6] This factor is not of much practical importance if the organism is truly sensitive and a larger dose of the drug is given. By and large, sulfadiazine remains the drug of choice, since it has fairly rapid absorption with fairly slow excretion and a minimum of toxic effects. Only 56 per cent is bound to plasma proteins. Toxicity and sensitivity are least found in the use of sulfadiazine and sulfamerazine.[7]

The development of resistance of organisms to drugs has long been recognized. It is important to remember that it is the organism, not the patient, which becomes resistant. The mechanism is not clearly understood, but it is thought to be the result of mutations occurring during the initial period of treatment which lead to the development of a few drug-fast organisms. These organisms survive and eventually predominate. The way to prevent this was pointed out by Ehrlich [8] years ago—the rapid elimination of the invading organisms before resistant strains have time to develop. This demands an adequate initial dose of

4. Swan, K. C.: Personal communication to the author.

5. Bellows, J. G.: Chemotherapy in Ophthalmology, Arch. Ophth. **29**:888 (June) 1943.

6. Davis, B. D.: Binding of Sulphonamides by Plasma Proteins, Science **95**: 78, 1942.

7. Goldstein, A.: Antibacterial Chemotherapy, New England J. Med. **240**:98, 1949.

8. Ehrlich, P.: Chemotherapeutische Trypanosomen-Studien, Berl. klin. Wchnschr. **44**:233, 1907.

the drug and perhaps the combination of two sulfonamides, so that organisms that develop a resistance to one drug will be knocked out by the other.[9] Thus, if the initial dose is 4 Gm., one might give 2 Gm. each of sulfadiazine and sulfamerazine, followed by 0.5 Gm. of each drug every four hours.

Owing to the indiscriminate use of sulfonamides and antibiotics for all sorts of minor infections, many resistant strains have been developed, and many persons have been rendered sensitive. In the Boston area it has been estimated that 30 per cent of all strains of staphylococci are

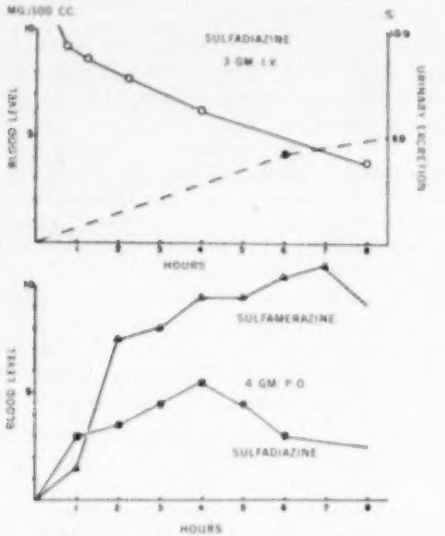

Chart 1.—Upper half: Blood levels, in milligrams per 100 cc. (solid curve), and cumulative urinary excretion, expressed as a percentage (broken curve), of sulfadiazine after single intravenous administration of 3 Gm. (data from Sadusk, J. F., and Tredway, J. B.: Yale J. Biol. & Med. **13**:539, 1941).

Lower half: blood levels, in milligrams per 100 cc. of sulfadiazine and sulfamerazine after single oral administrations of 4 Gm. (data from Bullowa, J. G. M., and Ratish, H. D.: J. Clin. Investigation **23**:676, 1944).

now penicillin resistant.[10] Generally speaking, the drugs should not be given unless the organism is known to be sensitive to them and the infection is severe enough to justify their use. Unless this rule is kept

9. Lehr, O.: Low Toxicity of Sulphonamide Mixtures, Proc. Soc. Exper. Biol. & Med. **64**:393, 1947.

10. Weinstein, L.: Personal communication to the author.

in mind, many patients may be unable to use them at a later date, when they may be needed as a life-saving measure.

The ocular diseases in which the sulfonamides are indicated are listed in table 1. In treatment of trachoma, inclusion blennorrhea and lymphogranuloma venereum they still remain the drugs of choice. In addition to these three virus diseases, they should be given in meningococcic meningitis and its ocular complications. In gonorrheal conjunctivitis they may be employed effectively when the patient is sensitive to penicillin or the strain is penicillin resistant. In all these diseases they should be used locally, as well as systemically—sodium sulfacetimide for local use and either sulfadiazine or sulfamerazine (or a combination of the two) for oral administration.

After perforating injuries and intraocular foreign bodies the sulfonamides should be given orally as a prophylactic measure on the chance

TABLE 1.—*Indications for Use of the Sulfonamides*

Drug of Choice in	Also Effective in
Trachoma	Gonorrheal conjunctivitis
Inclusion blennorrhea	Diplococcus pneumoniae infections
Lymphogranuloma venereum	Escherichia coli infections
Cerebrospinal meningitis	Hemophilus influenzae infections
	Beta hemolytic Streptococcus infections
	Actinomycosis
	Brucellosis (with streptomycin)
	Anthrax

that the potential infecting organism may be sensitive to them. They may be combined with the parenteral administration of penicillin or some other antibiotic if one wishes, but the sulfonamides will diffuse into the intraocular fluids more readily than other systemically given drugs.

THE ANTIBIOTICS

The literature on the various antibiotics has been voluminous, and new substances are being developed rapidly. The four best known are penicillin, streptomycin, aureomycin and chloramphenicol (chloromycetin®). Their mode of action is not as well understood as that of the sulfonamides, but presumably they interfere with certain enzyme systems necessary for the life of some bacteria and viruses. Most of them are absorbed more slowly and excreted more rapidly than the sulfonamides. In the case of penicillin (chart 2) this rapid excretion represented a real problem and led to the development of methods of administration designed to hold the drug in body depots so that it might be released continuously over a period of hours (chart 3). However, the antibiotics are generally superior to the sulfonamides for the following reasons: (1) They are usually less toxic; (2) their antibacterial action

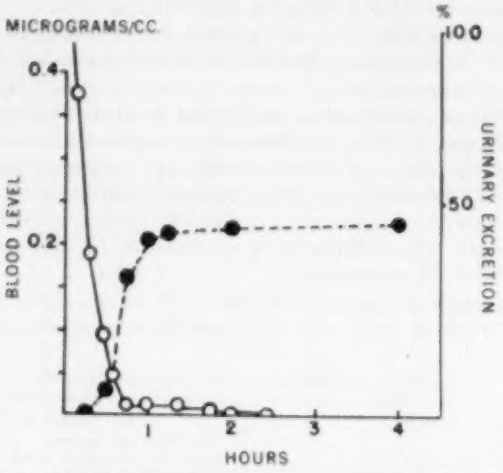

Chart 2.—Blood levels, expressed in micrograms per cubic centimeter (solid curve), and cumulative urinary excretion, expressed as a percentage (broken curve), of penicillin G after single intravenous administration of 12 mg. (adapted from data of Rammelkamp, C. H., and Keefer, C. S.: J. Clin. Investigation **22**:425, 1943).

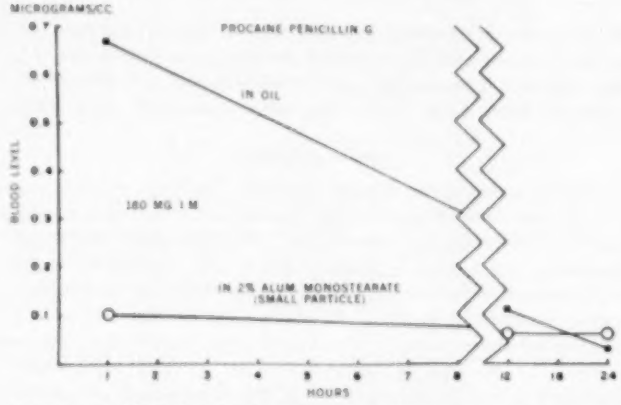

Chart 3.—Penicillin blood levels, expressed as micrograms per cubic centimeter, after single intramuscular administration of two new repository products (data of Thomas, E. W., and others: Newer Repository Penicillin Products, J. A. M. A. **137**:1517 [Aug. 21] 1948).

is not inhibited by autolytic products and secretions; (3) they have a less deleterious effect on the regeneration of corneal epithelium; (4) they have a greater range of antibacterial activity. With these advantages, they should be the drugs of choice in the treatment of ocular infections known to be due to organisms which are sensitive to them.

However, unless certain basic facts are understood regarding their distribution in the ocular tissues by various methods of administration, many patients will not be treated effectively, and much valuable time will be lost before the ocular infection can be brought under control.

Penicillin.—It is well known that penicillin given intravenously or intramuscularly does not penetrate well into the aqueous or vitreous of the normal eye. Von Sallmann [11] has shown this to be due partly to the functional state of the capillaries in the ciliary body and partly to the rapid excretion of the drug. Theoretically, the effect of parenteral administration of penicillin on intraocular infections is negligible unless very large doses are given and some attempt is made to increase the permeability of the capillaries of the ciliary body, as by paracentesis. Actually, the permeability of the capillaries of the ciliary body is increased in most infections of the anterior segment, permitting small amounts of penicillin to enter the aqueous. In infections of the posterior segment it appears to be impossible to get any penicillin into the vitreous by parenteral administration and, according to von Sallmann,[11] only a direct intravitreal injection of 0.1 cc. of pure penicillin G, containing not more than 1,000 units, will suffice. Care should be taken to deliver the drug at the center of the vitreous body, avoiding contact with the retina. Penicillin K should never be used, as it causes serious retinal atrophy.

Subconjunctival injections are capable of getting some penicillin into the aqueous, but only small amounts have been found in the vitreous.[12] If this method is used, a large amount of the drug is carried off by the blood vessels; moreover, it is very irritating unless combined with procaine. A much more direct attack is the injection of 0.1 cc. of pure penicillin G, containing not more than 1,000 units, directly into the anterior chamber. This is indicated particularly in cases of infections following perforations of the cornea with damage to the lens.

The local use of penicillin drops, while excellent in certain cases of conjunctivitis, will not be effective in obtaining adequate concentrations in the aqueous in the presence of an intact corneal epithelium.[13] Swan [14]

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11. von Sallmann, L.: Controversial Points in Penicillin Therapy in Ocular Disease, Arch. Ophth. **39**:752 (June) 1948.

12. Struble, G. C., and Bellows, J. G.: Studies on Distribution of Penicillin in the Eye and Its Clinical Application, J. A. M. A. **125**:685 (July 8) 1944.

13. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into Eye, Arch. Ophth. **31**:1 (Jan.) 1944.

14. Swan, K. C.: Personal communication to the author.

has pointed out that better results are obtained when the ointment base is used. He explains this by the "law of relative affinities." By this is meant that penicillin salts have a greater affinity for their aqueous vehicle than for the lipid barrier of the corneal epithelium and hence tend to remain in their vehicle. When they are prescribed in a base of anhydrous petrolatum, however, they have a greater affinity for the cornea than for the base and thus penetrate readily. Of course, if the epithelium is abraded, the corneal permeability is altered, and even aqueous solutions penetrate easily.[15]

Saturated cotton pack under the lid, the corneal bath and iontophoresis have all been shown experimentally to produce increased concentrations in the cornea and aqueous.[15]

The weight of experimental evidence and clinical experience indicates that the intramuscular administration of penicillin has its greatest value

TABLE 2.—*Indications for Use of Penicillin*

Drug of Choice in	Also Effective in
Gonorrheal conjunctivitis	Diphtheritic conjunctivitis
Staphylococcic infections	Cerebrospinal meningitis
Alpha hemolytic Streptococcus infections	
Beta hemolytic Streptococcus infections	
D. pneumoniae infections	
Syphilis	
Actinomycosis	
Anthrax	

in treatment of infections of the orbit and lid. When the cornea or intraocular chambers are involved, the drug should be used locally by one of the methods already mentioned.

It should not be forgotten that adequate blood levels may be obtained by the oral use of penicillin provided the dose is large enough. Administration of 200,000 units by mouth four times a day will usually be sufficient. This method is expensive but may be used to advantage in children, obviating the use of a needle.

Table 2 gives a list of the ocular conditions in which penicillin may be employed.

Streptomycin.—This substance is especially effective against certain gram-negative and acid-fast organisms. It is very stable and is not excreted as rapidly as is penicillin (chart 4). It has the disadvantage of being toxic to the eighth nerve and the vestibular apparatus. For this reason it should not be administered systemically for longer than two or

15. Leopold, I., and LaMotte, W. O., Jr.: Penetration of Penicillin in Rabbit Eyes with Normal Inflamed and Abraded Corneas, Arch. Ophth. **33**:43 (Jan.) 1945.

three weeks at a time. It is poorly absorbed orally and must be given parenterally. Dihydrostreptomycin is less likely to be toxic and will probably replace streptomycin eventually. Another disadvantage of streptomycin is its pronounced tendency to produce resistant strains, much more than does penicillin. Like penicillin, it penetrates poorly into the vitreous after parenteral administration but penetrates the aqueous somewhat better.[16] Its local use has the disadvantage of retarding regeneration of corneal epithelium. It will not penetrate the corneal epithelium when the latter is intact but will do so readily when ulcer formation is present. It is very useful in combating certain corneal infections due to gram-negative organisms. When applied locally in the

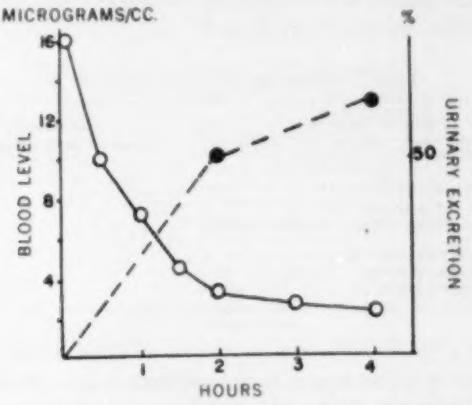

Chart 4.—Blood levels, expressed as micrograms per cubic centimeter (solid curve), and cumulative urinary excretion, expressed as a percentage (broken curve) of streptomycin after single intravenous administration of 100 mg. (adapted from the data of Adcock, J. D., and Hettig, R. A.: Absorption, Distribution and Excretion of Streptomycin, Arch. Int. Med. **77**:179 [Feb.] 1946).

form of drops (50 mg. of base per cubic centimeter) or by corneal bath, it is the drug of choice in the treatment of Bacillus pyocyaneus ulcer of the cornea. Iontophoresis is even more effective in obtaining high concentrations in the cornea. Several cases have been reported in which direct intravitreal injection of 1,000 micrograms has been successfully

16. Bellows, J. G., and Farmer, C. J.: Streptomycin in Ophthalmology, Am. J. Ophth. **30**:1215, 1947. McDermott, W.: Toxicity of Streptomycin, Am. J. Med. **2**:491, 1947. Marshall, E. K., Jr.: Absorption, Distribution, and Excretion of Streptomycin, J. Pharmacol. & Exper. Therap. **92**:43, 1948. Chandler, C. A., and Schoenbach, E. B.: Studies on Bacterial Resistance to Streptomycin, Proc. Soc. Exper. Biol. & Med. **64**:208, 1947.

employed to combat infections of the posterior segment without undue damage to the retina. Its greatest use however, appears to be in combating ocular tuberculosis. Woods [17] has shown, both experimentally and clinically, that when combined with promizole® (4,2-diaminophenyl-5'-thiazolsulfone) this drug gives excellent results. We have tried these drugs in several cases of choroiditis believed to be tuberculous in origin and can confirm Woods's claims. The dose recommended is 0.5 Gm. of streptomycin given parenterally twice a day combined with 6 Gm. of promizole® given orally daily in divided doses. The drugs are given for a period of three weeks only and their use is stopped on the first toxic manifestation.

The oral use of paraaminosalicylic acid,[18] 12 Gm. daily in divided doses, in combination with streptomycin has proved equally effective, and we now prefer this drug to promizole.®

TABLE 3.—*Indications for Use of Streptomycin*

Drug of Choice in	Also Effective in
Tuberculosis (with sulfones or paraaminosalicylic acid)	Brucellosis (with sulfonamides)
Tularemia	
B. pyocyaneous ulcer	
Escherichia coli infections	
Hemophilus duplex (Morax-Axenfeldt bacillus) infections	
H. influenzae infections	
Bacillus subtilis infections	
Proteus vulgaris infections	

Table 3 gives the indications for the use of streptomycin.

Aureomycin.—This drug is being recognized as very effective against many infections with gram-positive and gram-negative organisms and some rickettsial diseases. Its effect on virus diseases is still controversial. It has the same shortcomings as have penicillin and streptomycin in that it penetrates poorly into the intraocular chambers after systemic administration and when used locally will not pass through an intact corneal epithelium.[19] Its local application may cause irritation of the eye if made

17. Woods, A. C., and Wood, R. M.: Studies in Experimental Ocular Tuberculosis: Effects of Streptomycin and "Promizole" on Experimental Ocular Tuberculosis in the Immune-Allergic Rabbit, Arch. Ophth. **40**:413 (Oct.) 1948. Woods, A. C.: Therapeutic Action of Streptomycin and Promizole® in Clinical Ocular Tuberculosis: A Preliminary Report, ibid. **42**:521 (Nov.) 1949.

18. Bietti, G. B.: Use of Paraaminosalicylic Acid Alone or in Association with Streptomycin in Ocular Tuberculosis: Experimental and Clinical Investigations, Arch. Ophth. **43**:431 (March) 1950.

19. Bellows, J. G.; Richardson, V., and Farmer, C. J.: Aureomycin in Ophthamology, Am. J. Ophth. **33**:273, 1950.

too frequently. The recommended local dose is a 0.5 per cent solution of aureomycin borate instilled every two to three hours. The substance is very unstable, and the solution must be freshly prepared, as it retains its potency only 48 hours in the ice box. A stable ointment preparation is now on the market. It retards regeneration of corneal epithelium, but less so than does streptomycin. Iontophoresis and subconjunctival injections have not been very successful in getting this drug into the aqueous and are definitely irritating.

Aureomycin is well absorbed from the gastrointestinal tract and can be used orally. Nausea and diarrhea are common side effects, but these can be minimized if food is taken beforehand.

Aureomycin appears to have a greater range of activity than the other antibiotics now in general use, and cases of sensitivity are rare. Many

TABLE 4.—*Indications for Use of Aureomycin*

Drug of Choice in	Also Effective in
Brucellosis	Gonorrheal conjunctivitis
Tularemia	Staphylococcic infections
	A. hem. strep. infections
	Beta hemolytic Streptococcus infections
	D. pneumoniae infections
	H. duplex (Morax-Axenfeldt bacillus) infections
	Inclusion blennorrhea
	H. influenzae infections
	Herpes simplex (?)
	Herpes zoster (?)
	Epidemic keratoconjunctivitis (?)
	Trachoma (?)

gram-positive and gram-negative organisms seem to be sensitive to it. Tularemia, brucellosis, trachoma and inclusion blennorrhea are said to respond favorably (table 4). It was hoped that all virus diseases might respond, but reports on its use in cases of herpes simplex, herpes zoster and epidemic keratoconjunctivitis are confusing. Swan [20] feels that all three of these diseases are favorably influenced by the early use of aureomycin, both locally and by systemic administration. Braley,[21] on the other hand, has had only fair clinical results in treatment of herpes zoster and epidemic keratoconjunctivitis, although, in his work with experimental animals, aureomycin appeared to afford protection from the herpes simplex virus. Our own results in herpes simplex and herpes zoster have certainly been disappointing. In a patient who was being treated with aureomycin for an infection of the bladder full-fledged

20. Swan, K. C.: Personal communication to the author.

21. Braley, A. E., and Sanders, M.: Aureomycin in Ocular Infections, Ann. New York Acad. Sc. **51**:221, 1948.

herpes zoster ophthalmicus developed during the course of treatment. Several cases of dendritic keratitis have not responded, and the results were not good in a case of trachoma. We have had no opportunity to treat patients with epidemic keratoconjunctivitis.

Chloramphenicol.—This is a new antibiotic which gives promise of being very useful. It is absorbed so rapidly from the stomach and excreted so slowly that parenteral injection is unnecessary. Its spectrum of antibacterial activity is about the same as that of aureomycin, but it has several advantages over the latter. It is not upsetting to the gastrointestinal tract, and Leopold and associates[22] have shown, in recent experimental studies, that it even penetrates well into the aqueous and vitreous after oral administration. This is an unusual and remarkable characteristic and is quite different from the properties of other antibiotics. Furthermore, it maintains its potency in solution for several weeks at room temperature. It can safely be injected into the aqueous or vitreous, but this would hardly be necessary in view of its capability of entering the intraocular fluids after oral use.

Locally, either an aqueous solution (2.5 mg. per cubic centimeter) is used, or the drug can be applied in ointment form (50 mg. per gram). It does not delay regeneration of the corneal epithelium, and it will penetrate into the aqueous through an intact corneal epithelium, either in aqueous solution or in ointment form. Cases of sensitivity are said to be rare, but I have seen one case of exfoliative dermatitis from its systemic use.

It will be seen from what has been said that the ophthalmologist of today has a wide choice of antibiotic agents. This complicates rather than simplifies his problem. He must withstand the temptation to prescribe these substances for minor ocular diseases that are self limited, but in case of the serious infections he must be prepared to choose the one best suited for the particular case. How is he to know? The answer is obvious. He must take a smear and make a Gram stain in cases of severe external infection. This takes only five minutes, and he then knows whether the organisms are gram-positive or gram-negative. If they are gram-positive, local penicillin therapy should be instituted; if gram-negative, streptomycin is indicated, unless clinical experience tells him he is dealing with a gonococcic infection, in which case penicillin should be used. At the same time, a culture should be made; this later will give him more specific information about the invading organisms. From this culture, sensitivity tests should be

22. Leopold, I. H.; Nichols, A. C., and Vogel, A. W.: Penetration of Chloramphenicol U. S. P. (Chloromycetin®) into the Eye, Arch. Ophth. **44**:22 (July) 1950.

made with the antibiotic in use to be certain that a bacteriostatic effect is present. For instance, a gram-positive organism may have been found in the smear and the patient placed under treatment with penicillin. The culture and sensitivity tests may then reveal that the organism is a resistant strain of Staphylococcus which grows well in a solution of penicillin. This information calls for an immediate change of treatment to aureomycin or chloramphenicol, or possibly to the sulfonamides, depending on which agent seems best fitted to deal with the particular organism.

In the case of intraocular infection, smears and cultures may be difficult to obtain, and reliance must be placed on a "shotgun prescription," in the hope that the situation will be taken care of. In such cases, perhaps oral use of chloramphenicol would be indicated, as the drug appears to be bacteriostatic to a number of gram-positive and gram-negative organisms. Furthermore, it is known to penetrate into the intraocular fluids. This, combined with sulfonamide therapy, would be a reasonable approach to a situation in which one is necessarily working in the dark.

THE ANTIHISTAMINICS

These substances comprise an interesting chapter in the book of therapeutics. Introduced in France a few years ago, the number of these compounds is constantly increasing. It is believed that they act by competing with histamine for the receptor cells, thereby nullifying the action of histamine on the tissues. Although there are many optimistic reports of their use in cases of ocular allergy, my own experience with them has, on the whole, been disappointing. They are certainly not effective in cases of nongranulomatous uveitis. I have had no success in treating several cases of vernal conjunctivitis.

In cases of periodic congestion of the conjunctiva, with itching and swelling of the lid margins, a condition thought to be due to an allergy, I have used antistine® (2-phenylbenzylaminomethyl-imidazoline) solution locally, with little success.

Leopold and his co-workers,[23] in the experimental type of anaphylactic uveitis produced by horse serum, found that tripelennamine pyrabenzamine® prevented the attack from developing if given intramuscularly prior to the intoxicating injection of horse serum. No beneficial effect was obtained, however, if the antihistaminic drug was given after the attack had developed.

This probably explains the failure of these drugs to work in most instances. Theoretically, they have the ability to replace histamine and

23. Leopold, I. H.: Dean, W., and Blazar, H.: An Evaluation of Antihistaminic Drug in Experimental Uveitis, Am. J. Ophth. **32**:31, 1949.

abort the attack if given just as the attack begins. But once the attack is well established they seem to be of little value.

I have found tripelennamine useful in preventing sneezing attacks during cataract surgery in patients prone to such attacks. I have given it for a full 24 hours beforehand (50 mg. four times a day) in several instances.

STEROIDS OF THE ADRENAL CORTEX

The use of certain steroids of the adrenal cortex and their activating hormones from the anterior lobe of the pituitary gland in the treatment of rheumatoid arthritis, gout and asthma seems to be a major therapeutic advance.[24] The employment of these substances in ocular disease has given rise to great hopes that the course of treatment-resisting entities will be shortened. Owing to unavailability of these hormones, there are only a few ophthalmologists in the country who have had the opportunity to treat a large number of patients. My own experience has not been extensive, but the results have been encouraging. Even though most ophthalmologists cannot obtain the drugs at present, it is interesting to speculate on the theories of how they act and to be cognizant of their limitations.

A number of steroids in the adrenal cortex are known to have a pronounced effect on the body metabolism. One in particular, cortisone (Kendall's compound E, or 17-hydroxy-11-dehydrocorticosterone), not only regulates the intermediary metabolism of proteins, fat and carbohydrates but also exerts a control on the bloodforming tissues of the body.[25] Apparently, these steroids can be released by the adrenal cortex by the action of the adrenocorticotropic hormone of the pituitary (ACTH), so that either the steroid itself or its activating hormone may produce similar results. The ACTH, however, may cause excessive hyperplasia of the adrenal cortex, and thus other physiological effects may occur, such as the androgenic effect leading to excessive masculinization, if therapy is long continued. The use of cortisone, on the other hand, may cause an atrophy of the adrenal cortex.[26]

Other complications resulting from therapy may be noted:

1. Water retention is common, resulting in pitting edema and gain in weight. A low salt diet should therefore be used to combat this tendency. Hypertensive cardiovascular disease may be aggravated.

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24. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever, and Certain Other Conditions: A Study in Clinical Physiology, Arch. Int. Med. **85**:545 (April) 1950.

25. Sprague, R. G., and others: Observations on Physiological Effects of Cortisone and ACTH in Man, Arch. Int. Med. **85**:199 (Feb.) 1950.

26. Thorn, G. W., and others: Medical Progress: The Clinical Usefulness of ACTH and Cortisone, New England J. Med. **242**:783, 1950.

2. Euphoria or mental depression is frequently noticed, especially the former.

3. Elevation of the blood pressure has occurred in some cases, especially with ACTH.

4. Transient glycosuria is not infrequent. At present the drugs appear to be contraindicated in diabetes.

5. Retardation of wound healing has been noted. Therefore no ocular surgery should be performed while the patient is under treatment.

Reports have been accumulating of the favorable action of cortisone and ACTH in the treatment of uveitis and other ocular inflammations.[27] The reason for this beneficial effect is not fully understood. It has been suggested by Thorn that adrenal steroids may block the hypersensitivity of body cells to bacterial and nonbacterial substances. It is known that when they are administered certain fundamental changes take place. 1. There occurs a characteristic hematological response, consisting of a decrease in the lymphocytes and eosinophils. 2. The blood glucose level rises. 3. There is an increased output of uric acid. Only recently Potts, Johnson and Goodman [28] have called attention to the similarity of the response in cases of uveitis treated with intravenous injection of typhoid vaccine. In 16 intravenous administrations of typhoid vaccine they found without exception the same response as that following ACTH therapy. They inferred that the good results of intravenous administration of typhoid vaccine are probably due to the stimulation of the adrenal cortex to produce cortisone, through stress reactions acting on the pituitary gland.

CONCLUSIONS

The past 15 years have brought forth a tremendous advance in the treatment of ocular infections. Those of us who are old enough can look back with no regret on the days when the nurseries were filled with cases of ophthalmia neonatorum and the wards crowded with cases of infected corneal ulcers and trachoma. Those days, fortunately, are behind us. We ophthalmologists have in our hands the means of controlling many diseases formerly fatal to vision, but we must be able to use them to their best advantage. The future is also bright. Startling

27. Gordon, D. M., and McLean, J. M.: Effects of ACTH Therapy in Ophthalmological Conditions, J. A. M. A. **142**:1271 (April 22) 1950. Olson, J. A., and others: Effect of ACTH on Certain Inflammatory Diseases of the Eye, ibid. **142**:1271 (April 22) 1950.

28. Potts, J.; Johnson, L. V.; Orchen, M., and Goodman, D.: Protein Transport in Ocular Structures, read before a Mid-Century Conference on Progress, National Society for the Prevention of Blindness and the Pan-American Association of Ophthalmology, Miami Beach, Fla., March 26-31, 1950, to be published.

new discoveries seem to indicate that many other resistant ocular diseases may be successfully controlled. But a word of warning should be spoken. The new drugs that will be made available to us may be likened to atomic energy. They are extremely powerful and capable of causing great damage unless we are cognizant of their potentialities and know how to employ them judiciously. It will take some time before the mechanism of their therapeutic action is understood and the dosage regulated so that important endocrine functions are not thrown too far out of balance. Let us not make the mistake of wishfully thinking that all disease will succumb to these hormones and prescribe them indiscriminately, without due appreciation of what we may be doing.

FACTORS INFLUENCING THE POSTOPERATIVE RESULTS IN CONCOMITANT CONVERGENT STRABISMUS

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IT IS UNDERSTANDABLE that the results of the surgical treatment of concomitant convergent strabismus are variable, for, as pointed out by Lancaster,[1] "Operation is a vicarious remedy. It does not cure by removing the cause but by substituting a different set of conditions with which the physiologic mechanism must work." Being in complete accord with this statement, we thought that an evaluation of end results could best be accomplished by an analysis of 79 cases of surgically treated concomitant convergent strabismus. All the patients in this series have been followed for at least seven years since operation, for it was felt that any shorter period was inadequate for an accurate determination of the final outcome. Since the number of cases is too small to permit statistical analysis, percentages are given only when they are of real significance. We shall point out some important steps in the preoperative examination and endeavor to show how improper diagnosis and treatment may influence the ultimate result.

PREOPERATIVE FACTORS

Refractive Error.—Foremost in importance is knowledge of the refractive error under complete cycloplegia. A good general rule is that the higher the hypermetropia, the more conservative should be the surgical treatment. This is particularly true of the esotropias, in which there is a hypermetropia of 4 D. or more, for even though the use of lenses does not immediately remove the entire deviation these imbalances gradually tend to decrease in amount and often disappear under

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1. Lancaster, W. B., in The Eye and Its Diseases, edited by C. Berens, Philadelphia, W. B. Saunders Company, 1949, p. 966.

conservative treatment. If operation is to be considered at all, it should be designed to remove only that portion of the squint not corrected by the prolonged use of lenses. Any surgical procedure in these cases is likely to be followed by a subsequent divergence. Of the 79 patients operated on for concomitant convergent strabismus and followed after operation for over seven years, only seven had more than 4 D. of hypermetropia.

The salient features of one such case history are of interest:

Jan. 18, 1936: E. G., aged 5 years, had had inward deviation of the left eye since the age of 1 year. Vision was 20/30 in the right eye and 20/200 in the left eye. ST measured 10△, and LHT, 5△, reaching 20△ with the eyes up and right. ST′ was 25△. Lateral deviation was reduced by glasses to ST 5△ and ST′ 15△, and there was no evidence of spasmodic inshoot when she was wearing lenses. Refraction with atropine cycloplegia was as follows:

R. E.: + 4.50 sph. ⌒ + 0.75 cyl., axis 90; vision 20/30
L. E.: + 5.00 sph. ⌒ + 1.25 cyl., axis 90; vision 20/200

Vision in the left eye after three months of constant occlusion was 20/40.

March 31, 1937: Operation consisted of 4 mm. of recession of the medial rectus muscle and myectomy of the inferior oblique muscle of the left eye.

Sept. 27, 1937: X T measured 10△, and X T′, 5△. Vision in the left eye was 20/100.

April 5, 1944: X T and X T′ measured 40△. Refraction was as follows:

R. E.: + 0.50 sph. ⌒ + 0.50 cyl., axis 90; vision 20/20
L. E.: + 0.75 sph. ⌒ + 1.00 cyl., axis 90; vision 20/100

Operation consisted of 4 mm. resection and reattachment of the medial rectus muscle combined with 3 mm. recession of the lateral rectus muscle of the left eye.

March 22, 1945: × T and × T′ measured 20△. There was no convergence. Reoperation was advised.

An analysis of this case illustrates the danger of subsequent outward deviation when only a relatively small operative procedure is carried out in the presence of high hypermetropia. It also shows the necessity for a lengthy period of observation. At the end of six months the result was satisfactory, but soon thereafter the outward deviation made its appearance and steadily increased in amount for seven years, at which time a secondary operation was performed. The change in the refractive error may have been a factor in this development; but the original good position of the eyes when wearing glasses, the amblyopia and the poor convergence should have been warnings against operative intervention.

Visual Acuity.—For many years it has been taught that the correction of a monocular convergent strabismus with poor vision in the deviating eye is an uncertain procedure. It is believed that many of these eyes subsequently turn out. Our studies indicate the truth of these statements, particularly when the operative procedure has been such as to destroy the ability to converge. In this series every effort was

made to secure the best possible vision in the squinting eye before proceeding with surgical correction. The results in 15 cases of monocular squint are evidence of the value of adequate occlusion. In eight of these 15 cases vision of 20/50 or better was maintained for more than seven years. In seven of these eight cases a satisfactory result was obtained, whereas in only one of the seven cases in which the vision did not improve did the eyes remain straight. Furthermore, in 10 of 13 cases of alternating squint the surgical treatment was successful. These figures are in sharp contrast to the results obtained in cases with poor vision in the squinting eye. In only 40 per cent of the latter was parallelism maintained at the end of seven years.

Deviation.—One of the most important considerations in the selection of the proper operative procedure is the amount of deviation present. The manner in which this is measured varies with the surgeon. We, personally, use prismatic measurements and feel that we can determine it with greater accuracy by this method than by any other. Regardless of how the amount of deviation is determined, it is agreed that it is important to know its variability in different directions of gaze and at different distances. While it is true that information gathered from such measurements is of inestimable value, it must be remembered that many other factors have to be considered before a proper operative selection can be made. For this reason, any attempt to reduce the surgical procedures to a mathematical equation based on measurements alone is destined to fail.

Fixing Eye.—The importance of determining the fixing eye has received scant attention. In true monocular deviations the fixing eye is obvious, but in the group of alternating squints it is more confusing. Indiscriminate fixation is rare, and most persons with so-called alternating strabismus have a definite preference for one eye in some particular direction of gaze. Roughly, these squints may be divided into the following groups: (1) indiscriminate fixation; (2) homonymous fixation; (3) heteronymous fixation.

In the so-called homonymous fixation the right eye is used on looking to the right and the left eye on looking to the left, whereas in the heteronymous type fixation is reversed. In our opinion, this subdivision, combined with knowledge of the near point of convergence, is of value in helping to select the correct operative procedure. Thus, persons with homonymous fixation generally have some spasm of convergence and respond well to bilateral recession. In contrast, patients with heteronymous fixation usually do not show any overaction of convergence but often have some limitation of outward motility. These patients tend to do better when the external rectus muscles are resected.

Near Point of Convergence.—Determination of the near point of convergence is conceded to be of value in helping to select the correct operative procedure, but it is important to reiterate the usefulness of this test. The present trend in muscle surgery is toward recession of the medial rectus for nearly every type of concomitant convergent strabismus. There is no doubt that the bilateral recession is a definite part of the ophthalmic surgeon's armamentarium, especially in infants with a high degree of squint; but the importance of a careful determination of the convergence near point before operation cannot be emphasized too strongly. All have seen cases in which the operative result is good for distance but, because of poor convergence or absence of convergence, an outward deviation occurs at closer ranges. This is most frequently the result of an indiscriminate or excessive recession performed in a case in which spasm or overaction of convergence was not a factor.

Rotations.—In addition to the measurement of the deviation, the fixing eye, the near point of convergence and the other factors already enumerated, the behavior of the eyes in the different directions of gaze, first with one eye fixing and then with the other, should be noted. This simple test affords valuable information, which serves to complete the picture. It is important to remember that limitation of motion in any particular direction of gaze can be due either to paresis or weakness of the particular muscle or to contracture or fibrosis of its direct antagonist. For example, after fracture of the floor of the orbit, there is often an apparent paralysis of the superior rectus, which in reality is due to the globe's being held down by adhesions around the inferior rectus muscle.

Vertical Deviations.—For many years there has been discussion on the importance of small vertical deviations in the presence of such greater lateral imbalances. White and Brown [2] have urged the correction of the vertical component before proceeding with any operation on the horizontal element. In contrast to this view, Burian,[3] Prangen,[4] Post [5] and others feel that these smaller vertical deviations can usually be ignored and that the initial operative procedure should be designed to remove the greater lateral squint. Within recent years it has been our policy to follow the latter suggestions. Having tried both approaches,

2. White, J. W., and Brown, H. W.: Occurrence of Vertical Anomalies Associated with Convergent and Divergent Anomalies, Arch. Ophth. **21**:999 (June) 1939.

3. Burian, H.: Surgery of Extraocular Muscles, Am. J. Ophth. **33**:380 (March); 577 (April) 1950.

4. Prangen, A. deH.: Some Observations on the Surgical Treatment of the Extra Ocular Muscles, Tr. Am. Ophth. Soc. **44**:251, 1947.

5. Post, L. T.: Suggestions for the Surgical Management of Strabismus, Am. J. Ophth. **33**:345, 1949.

we believe that in general it is more satisfactory to remove the lateral component first and then, if necessary, correct the residual vertical deviation. Of the present series of cases of convergent strabismus, a vertical component was present in approximately 50 per cent (44 of the 79). The postoperative results in the latter did not differ materially from those in which no vertical imbalance was demonstrable. In some instances, after operation on the horizontal deviation, the vertical component remained unchanged, without subsequent development of any lateral imbalance. If only monocular vision can be expected, it has been our policy to ignore the vertical element unless it is sufficient to be of cosmetic importance. If one has reason to hope for binocular vision and the vertical deviation is small in amount, we believe that the initial operative procedure should be confined to the lateral deviation. On the other hand, if both lateral and vertical deviations are considerable in amount, we have often removed them simultaneously.

Retinal Correspondence.—Abnormal retinal correspondence was found by Adler and Jackson [6] in 64 per cent of the cases of convergent squint that they followed. Travers [7] found the condition in 50 to 60 per cent of all cases of squint, and Deborah Dicke [8] reports abnormal retinal correspondence in 71 per cent of cases. However, as pointed out by Pyangen,[4] and more recently by Burian [9] and Travers,[10] the presence or absence of abnormal retinal correspondence has little effect on the surgical result. Travers does not believe that abnormal retinal correspondence will force the eyes back to their preoperative position, nor does he think that fusion is necessarily a restraining force. He states that abnormal retinal correspondence is nearly always present in cases of squint of more than 20 degrees and believes that operation is the only treatment which will alter this condition. According to this author, surgical correction should be made before the age of 3 years if one wishes normal retinal correspondence to develop. Bressler [11] found normal postoperative retinal correspondence in 8 per cent of cases showing abnormal retinal correspondence before operation. Hicks and

6. Adler, F. H., and Jackson, F. E.: Correlations Between Sensory and Motor Disturbance in Convergent Squint, Arch. Ophth. **38**:289 (Sept.) 1947.

7. Travers, T. a'B.: The Comparisons Between the Visual Results Obtained by Various Methods Employed for the Treatment of Concomitant Strabismus, London, George Pulman & Sons, Ltd., 1936, p. 34.

8. Dicke, D.: Abnormal Retinal Correspondence, Am. J. Ophth. **25**:585 (May) 1942.

9. Burian, H.: Strabismus: Review of the Literature, Arch. Ophth. **44**:146 (July) 1950.

10. Travers, T. a'B.: The Practical Importance of Abnormal Retinal Correspondence, Tr. Am. Acad. Ophth. **54**:561, 1950.

11. Bressler, J. L.: Treatment of Strabismus, Arch. Ophth. **16**:433 (Sept.) 1936.

Hosford [12] reported that in 66 per cent of 24 cases studied fusion developed after operation. Therefore, it is generally agreed that normal retinal correspondence may develop spontaneously after operation.

It was not possible to test retinal correspondence and fusion in all the 79 cases of convergent strabismus. However, fusion of some degree was present after operation in at least 25 per cent of them. The presence or absence of fusion apparently made little difference in the final position of the eyes. Even though our cases were not studied primarily from this point of view, our experience tends to support Burian's [9] and Travers' [10] views. In a few instances abnormal retinal correspondence was observed to change spontaneously to normal retinal correspondence after operation. We believe, therefore, that the development of normal retinal correspondence and of fusion is aided by proper alinement of the eyes, sometimes being the consequence rather than the cause of a good surgical result.

Orthoptics.—A much discussed question is the role of orthoptic training, both before and after operation. Judging from the literature, it is an aid in stabilizing the results of surgical correction. Bressler,[11] in 1936, reported that 81 per cent of his patients developed fusion and 56 per cent straight eyes if preoperative and postoperative orthoptic exercises were combined with surgical treatment. Good results have also been reported by Berens, Elliot and Sobacke [13]; Lordan [14]; Faulkner, Scully and Carter,[15] and others. A few authors have found postoperative orthoptic exercises of little help. Thus, Duthie [16] believes that while postoperative orthoptic exercises do not help residual deviations of 5 to 10 degrees, the establishment of fusion before operation decreases the risk of secondary divergence. The latter view is also stressed by Post.[5] Prangen [4] states that one should avoid exercises in the case of adults with postoperative diplopia and persistent inability to fuse. We firmly believe that defective fusion is more troublesome than absence of fusion. Such a patient is in constant conflict between suppression and binocular vision, and this often makes him most unhappy. As we see it today, many men expect orthoptic training to do the impossible. First, they look for it to cure the nonaccommodative type of squint;

12. Hicks, A. M., and Hosford, G. N.: Orthoptic Treatment of Squint, Arch. Ophth. **13**:1026 (June) 1935.

13. Berens, C.; Elliot, A. J., and Sobacke, L.: Orthoptic Treatment and the Surgical Correction of Strabismus, Am. J. Ophth. **24**:1418, 1941.

14. Lordan, J. P.: Orthoptic and Surgical Management of Strabismus, Arch. Ophth. **12**:843 (Dec.) 1934.

15. Faulkner, S. H.; Scully, E., and Carter, E. E.: Operation on 100 Cases of Convergent Concomitant Squint, Brit. J. Ophth. **28**:403, 1944.

16. Duthie, O. M.: Operative Impressions in Orthoptic Training, Brit. Orthoptic J. **1**:28, 1939.

then they expect the orthoptic technician to correct a residual deviation (either overcorrection or undercorrection) which is directly the result of injudicious surgical correction. To us, the role of orthoptics is that of an adjuvant, but no more. It can be of assistance if employed with a modicum of common sense; if not, it is capable of doing much harm.

SURGICAL FACTORS

Having reviewed the preoperative findings which we consider necessary for selection of the correct surgical procedure, it is proper that we discuss causes of failure.

There are two factors in surgical technic to which operative failures are usually attributed, viz., slipping sutures and excessive adhesions. As far as we have been able to tell, poor results have not occurred from slipping sutures. Although Onfray and St. Martin [17] believe this slipping is the most frequent cause of a poor result after an advancement, the experimental findings of Carroll and Blake [18] and of Chouke [19] are not in accord with this view. These men found considerable foreign body reaction and exudate around the suture material within 48 hours, and at the end of three to four days a large amount of fibroblastic infiltration was present in these areas. It is our belief, therefore, that if the muscle is in proper position at the close of the operation no fear need be entertained about subsequent slipping of the sutures. Nor can we agree with Gifford [20] that postoperative rotation of the eyes may be responsible for an apparent change in the position of reinsertion. It is true that occasionally on reexposure of a receded muscle we find it reattached at its original site. This we think is the result of faulty technic at the time of the first operation. In these cases the surgeon had inadvertently placed the sutures too far posteriorly in the muscle, thus allowing the free end of the tendon to reattach itself at the original site.

In our experience, the most frequent factor in surgical technic that leads to a poor result is postoperative adhesions. These may result in overcorrection or in undercorrection. As Gifford [20] has pointed out, on performing a secondary operation, one often finds extensive adhesions about muscles on which operation has previously been performed. These sometimes extend well behind the equator. Here, increased

17. Onfray, and St. Martin, cited by Dejean, C.: Le réglage de l'opération du strabisme, Arch. d'opht. **6**:1, 1946.

18. Carroll, F. D., and Blake, E. M.: Repair Following Operations on Extra-Ocular Muscles: Histologic Obervations, Arch. Ophth. **8**:711 (Nov.) 1932.

19. Chouke, K. S.: Repair Following Tucking Operations on the Extraocular Muscles, Am. J. Ophth. **28**:50 (Jan.) 1945.

20. Gifford, S. R.: Position of Muscles After Operation for Strabismus, Arch. Ophth. **27**:443 (March) 1942.

trauma and excessive bleeding seem to be the most important causative factors. The presence of such adhesions can usually be elicited by passive rotation of the globe with forceps. Resistance to this maneuver is proof positive of their existence.

SECONDARY OPERATIONS

It has already been seen that either an overcorrection or an undercorrection can result from the improper selection of the original procedure. While this is probably the commonest reason for failure, poor results do occur from other causes. Overcorrection may also be due to (1) too extensive an operation, or (2) postoperative adhesions. If shortening of a rectus muscle has been combined with a recession of its direct antagonist, limitation of motility in the field of action of the receded muscle may be due to any, or all, of the following causes: (1) cicatricial tissue around the shortened muscle, mechanically preventing free motility in the opposite fields; (2) nonfunction of the receded muscle because its insertion has been placed too far posteriorly, and (3) adhesions around the receded muscle, interfering with its action. Therefore, in operation in a case of overcorrection no rule-of-thumb procedure can be used. It is necessary to determine by exposure of both the muscles previously operated on which of these conditions prevail and to proceed accordingly. In our experience, an operation to correct an overcorrection has to be more extensive than the original one. Many of these secondary operations result in little or no improvement unless particular attention is directed toward the above-named factors. To overcorrect a secondary divergence is unusual. In 13 such cases included in this series it did not occur a single time, whereas in six of these 13 cases the second operation did not entirely remove the outward deviation.

The problem of treating an undercorrection is somewhat different. The two factors involved are (1) inadequate primary operation and (2) adhesions. If the surgeon can exclude the presence of adhesions, which, as already stated, can be done by employing passive rotation and inspection of the previous operative sites, he can be reasonably sure that the first procedure was insufficient. However, having decided this point, he should proceed most cautiously, because secondary resections and recessions appear to produce much more correction than do these operations when used as the primary procedure. The reason for this is not clear, but we suspect that the presence of adhesions and the weakening of the convergence power are the chief factors. Especially in operations aimed at correcting a residual deviation of 15 Δ or less, extreme caution has to be exercised, and particular attention must be given to the near point of convergence if one is to avoid a distressing overcorrection. Of 24 cases in which the initial operation resulted in an undercorrection, the secondary procedure produced an overcorrection in

10. In eight of these 24 cases the secondary procedure was entirely successful, whereas in six some undercorrection remained. In view of these results, it would seem logical to argue not only that the initial procedure should be adequate but also that even greater care should be exercised in removing these residual undercorrections.

SUMMARY

The over-all statistics in this series of 79 cases of concomitant convergent strabismus at least seven years after operation were as follows:

	No. of Cases
Deviation less than 10△	44 (56%)
Outward deviation more than 10△	16 (20%)
Inward deviation more than 10△	19 (24%)

This period of postoperative observation was selected because it was felt that with any shorter one the results would be misleading. The criteria used in determining the type of result obtained were prismatic measurements of the residual deviations. Patients presenting less than 10 D. of either esotropia or exotropia were considered to have a satisfactory result, whereas for all showing a deviation greater than this amount for either distance or near the result was classified as unsuccessful. In many cases of a so-called unsuccessful operation the cosmetic result was satisfactory to the patient, whereas in others the result was an obvious failure. Particular attention is given to the factors which have influenced these poor results. Foremost among them is the presence of low visual acuity in the squinting eye. In quite a number of these cases the operative result was good for two years or more; then a distressing divergence appeared. In almost all of this group the only immediate postoperative finding of significance was a remote near point of convergence. The presence of 4 D. or more of hypermetropia seemed to increase this tendency to secondary divergence. On the basis of this study, neither the age of the patient nor the duration of the squint is an important factor in the postoperative result. In our opinion, the degree of squint affects only the extent of operative intervention required to bring about its removal. Selection of the operative procedure by a mathematical formula is unsatisfactory because many factors in addition to the degree of deviation have to be considered. Besides the refractive error, visual acuity and near point of convergence, the fixing eye and the movements of the eyes in the different directions of gaze are important preoperative considerations. The presence of abnormal retinal correspondence is not a contraindication to operation, nor does its persistence after operation greatly influence the ultimate position of the eyes.

On the basis on our observations, it seems wiser to defer consideration of a small vertical component until the larger lateral one has been

removed. Only in those cases in which the vertical element equals or exceeds the inward deviation do we feel that its correction should be part of the initial procedure. The value of orthopic treatment is still undecided, but as a postoperative measure it cannot be expected to do more than stabilize the result. Secondary operations were performed on 22 of the 79 cases. The impressions gained from a study of these cases are (1) that overcorrections demand more radical treatment than original deviations, and that (2) undercorrections, particularly if moderate in amount, must be treated most cautiously. Most poor results are produced either by injudicious selection or by postoperative adhesions, and not by subsequent slipping of the sutures. Firm adhesions occur after excessive trauma at the time of the original operation and are most difficult to combat.

OPHTHALMOLOGIC FINDINGS IN SPONTANEOUS THROMBOSIS OF THE CAROTID ARTERIES

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AND
E. S. GURDJIAN, M.D.
DETROIT

ALTHOUGH traumatic or surgical occlusion of one or both common carotid arteries or their branches may be asymptomatic, especially in young persons, spontaneous thrombosis of these vessels in a subject with marked vascular sclerosis is more likely to lead to serious neurologic disturbances. Recent experience with three patients having optic nerve atrophy accompanying proved spontaneous thrombosis of the carotid arteries has prompted this communication.

The cause of spontaneous thrombosis of the carotid arteries is generally considered to be atherosclerosis. The thrombosis is commonly associated with sclerosis of the aorta and with aortic aneurysms. However, cases have been reported in which the cause of the thrombosis was thought to be obliterative syphilitic arteritis, embolism or nonsyphilitic arteritis.

The recent reports of Galdston and associates,[1] Wolfe,[2] Erickson[3] and Webster, Dolgoff and Gurdjian,[4] (the last of which included two of the present cases) show that advanced atheromatous changes are present in the carotid vessels. Sclerosis of the carotid arteries has been found even in young adults.

This study was aided by the Kresge Fund.

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1. Galdston, M.; Govons, S.; Wortis, S. B.; Steele, J. M., and Taylor, H. K.: Thrombosis of the Common, Internal and External Carotid Arteries: Report of 2 Cases with a Review of the Literature, Arch. Int. Med. **67**:1162 (June) 1941.

2. Wolfe, H. R. I.: Unexplained Thrombosis of the Internal Carotid Artery, Lancet **2**:567, 1948.

3. Erickson, S.: Über Arteriographie bei Thrombose in der Carotis interna, Acta radiol. **24**:392, 1943.

4. Webster, J. E.; Dolgoff, S., and Gurdjian, E. S.: Spontaneous Thrombosis of the Carotid Arteries in the Neck: Report of 4 Cases, Arch. Neurol. & Psychiat. **63**:942 (June) 1950.

In 11 cases gathered by Galdston and associates [1] the ages varied from 23 to 66 years, the average being 47 years. The literature indicates an age variation of from 7 to 71 years. The greatest frequency is found between 20 and 60 years, with a rather even distribution throughout this period. The sex incidence shows a ratio of 3.5:1, with males predominating. Involvement of the left carotid artery is 6.5 times as frequent as that of the right, a difference attributed by most authors to variations in the origin of the two carotid arteries.

The most marked sclerosis in the carotid arteries is found just below the point of bifurcation. Keele,[5] in a study of the pathological changes in the carotid vessels, found the carotid sinus to be next in order of frequency of involvement and the common carotid trunk next, with involvement of the external carotid artery rare. He found no involvement of the cervical portion of the internal carotid artery, but Dow [6] and Saphir [7] noted appreciable changes in the internal carotid artery in its course through the carotid canal and the cavernous sinus. The same degree of sclerosis was usually present in the aortic arch and bifurcations of the innominate and common iliac arteries as in the carotid sinus and the upper end of the common carotid artery in Keele's studies.

Whether the thrombosis is ascending from the atheromatous carotid complex or descending from terminal branches in the brain has not been established with certainty. Although the former is reasonable, the latter is quite possible, as was demonstrated in one case within our experience.

W. C., a white man aged 41, was admitted to Grace Hospital, with complaints of weakness of the right side of the body, headache and visual disturbance. Six days before admisson he collapsed at work, becoming unconscious. On recovering, he noted right hemiplegia with aphasia and inability to see to his right side. Gradual improvement followed in motor power and speech but not in vision. This episode was similar to three previous ones, the first of which occurred two years prior to his admission. It consisted of sudden paralysis with aphasia, but without any visual disturbance. The patient was hospitalized. Improvement was rapid. The other two episodes were transient and did not require hospitalization. The patient was able to continue at his work.

Studies made at the time of the first episode did not reveal hypertensive vascular disease. An electroencephalogram showed disorganized high voltage 7 per second waves in all areas on the left side. There were no ophthalmic abnormalities. An angiogram revealed failure of filling of the carotid branches, the carotid siphon being clearly visualized (fig. 1*A*).

Studies repeated two years later during the second, and present, hospitalization, showed recurrent hemiparesis with signs referable to the pyramidal tract. A right

5. Keele, C. A.: Pathological Changes in the Carotid Sinus and Their Relationship to Hypertension, Quart. J. Med. **2**:213, 1933.

6. Dow, D. R.: The Incidence of Arteriosclerosis in the Arteries of the Body, Brit. M. J. **2**:162, 1925.

7. Saphir, O.: Serpentine Aneurysm of the Internal Carotid Artery with Resulting Encephalomalacia and Cerebral Hemorrhage, Arch. Path. **20**:36 (July) 1935.

homonymous hemianopsia had been added. Laboratory studies showed no other alterations. Most significant, however, was the change found in the angiogram taken at this time. The carotid artery could be visualized only several centimeters beyond the bifurcation (fig. 1 *B*). It was believed that the occlusive process had progressed from the smaller carotid branches to the cervical portion of the artery as a descending thrombosis.

The symptoms of thrombosis of one or more carotid arteries are varied. Premonitory headaches, vertigo, hemiparesis, hemiparesthesia and speech defects may occur. Gross neurological changes appear. Temporary blindness, attributable to vasospasm, is not infrequent. The pupil on the side of the thrombosis may be transiently miotic. Nystag-

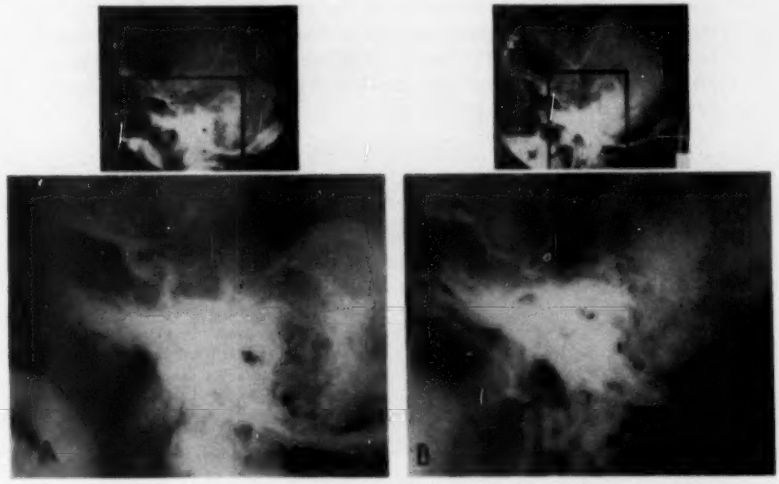

Fig. 1 (W. C.).—Obstruction of the middle cerebral artery (*A*), followed by proximal thrombosis of the cervical portion of the internal carotid artery (*B*).

mus may be found. Transient diplopia has been reported. Thrombosis of a central retinal artery, leading to optic nerve atrophy, may occur. Webster, Dolgoff and Gurdjian [4] classified cases of carotid thrombosis according to symptoms under four types: (1) an explosive form, simulating the usual cerebrovascular accident; (2) a slowly progressive type; (3) thrombosis with visual symptoms, and (4) a form without signs or symptoms. In this paper we are particularly concerned with the third group.

The diagnosis of thrombosis of the carotid artery may be suspected when the arterial pulsation is diminished or absent. It can be confirmed by angiograms and by surgical exploration.

Transient or intermittent diminution or loss of vision has been reported by Marinesco and Kreindler,[8] Kussmaul[9] and Harbitz.[10] This visual loss may be attributable to vasospasm. It is interesting that this symptom persisted for two days in the case reported by Marinesco and Kreindler without permanent visual loss.

Gradual visual diminution with subsequent partial optic nerve atrophy occurred in a case described by Raeder,[11] similar to one of the cases presented here. Most commonly there is sudden unilateral blindness with subsequent complete atrophy of the optic nerve. The first case of this type was reported by Penzoldt [12] in 1881. Abrupt unilateral blindness was followed by optic nerve atrophy and hemiplegia. Subsequent autopsy revealed thrombosis of the right common and internal carotid arteries with a large area of softening in the right cerebral hemisphere. Kussmaul[9]; Hunt [13]; Guthrie and Mayou,[14] and Egas Moniz, Almeida Lima and de Lacerda [15] reported other cases of unilateral optic nerve atrophy.

REPORT OF CASES

Case 1.—F. L. L., a white man aged 24, a laborer, was admitted to the Veterans Administration Hospital, Dearborn, Mich., on Sept. 9, 1948, with paralysis of the left arm and leg, blindness in the right eye and impairment of memory, all of approximately four months' duration. He stated that he had been in good health until the morning of May 15, 1948, when he awoke and found that he was unable to use his left arm and leg. At the same time he had severe frontal headache, which persisted almost six weeks. With the inability to use the left upper and lower extremities, he noted diminished sensation in these limbs, impairment of memory and confusion. During the ensuing weeks he was seen by several physicians and was informed that he had had a "stroke." Early in the course of his illness he became aware of visual impairment while reading and was subsequently informed by a physician that he was "blind in the right eye." He gradually acquired restricted power with spasticity in the left upper and lower extremities.

8. Marinesco, G., and Kreindler, A.: Oblitération progressive et complète des deux carotides primitives: Accès épileptiques; considérations sur le rôle des sinus carotidiens dans la pathogénie de l'accès épileptique, Presse méd. **44**:833, 1936.

9. Kussmaul, A.: Zwei Fälle von spontaner, allmäliger Verschliessung grosser Halsarterienstämme, Deutsche Klin. **24**:461 and 473, 1872.

10. Harbitz, F.: Bilateral Carotid Arteritis, Arch. Path. **1**:499, 1926.

11. Raeder, J. G.: Ein Fall von symmetrischer Karotisaffektion mit präseniler Katarakt und "Glaukom" sowie Gesichtsatrophie, Klin. Monatsbl. f. Augenh. **78**:63, 1927.

12. Penzoldt, F.: Über Thrombose (autochthone oder embolische) der Carotis, Deutsches Arch. f. klin. Med. **28**:80, 1880-1881.

13. Hunt, R.: The Role of the Carotid Arteries in the Causation of Vascular Lesions of the Brain, with Remarks on Certain Special Features of the Symptomatology, Am. J. M. Sc. **147**:704, 1914.

14. Guthrie, L. G., and Mayou, S.: Right Hemiplegia and Atrophy of Left Optic Nerve, Proc. Roy. Soc. Med. **1**:180, 1907-1908.

15. Egas Moniz; Almeida Lima, and de Lacerda, R.: Hémiplégies par thrombose de la carotide interne, Presse méd. **45**:977, 1937.

The patient walked with a typical spastic hemiplegic gait. Confirmatory signs referable to the pyramidal tract were present on the left side of the body. There was absence of pulsations in the right carotid and temporal arteries. The blood pressure was 90 mm. systolic and 68 mm. diastolic in each upper extremity. Inspection of the right fundus revealed a pale disk with distinct margins. The arteries and veins were uniformly narrowed. The left fundus was normal. Visual acuity was nil in the right eye and 20/20 in the left eye, with a left hemianoptic defect. Audiometric examination revealed 5 per cent loss of hearing in the right ear. Sensation was diminished in all modalities on the paralyzed side. A Wechsler-Bellevue intelligence test showed 13.7 per cent mental deterioration, and the findings on psychometric examination were "highly suggestive of an organic disturbance in the brain." The results of all laboratory tests, as well as the roentgenograms and the electrocardiogram, were normal. The spinal fluid was normal except for a protein content of 57 mg. per 100 cc.

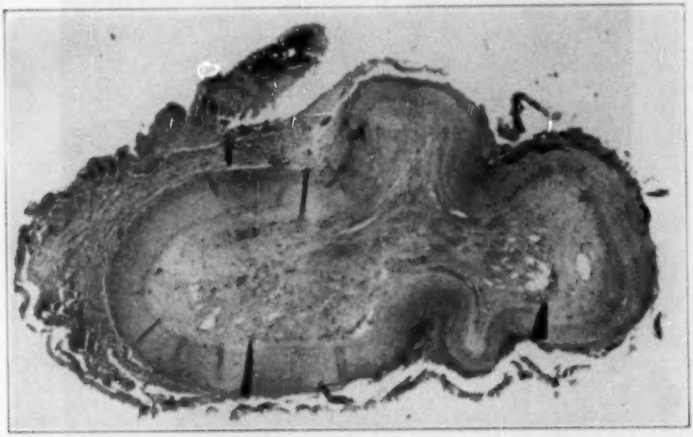

Fig. 2 (case 1).—Cross section of the bifurcation of the common carotid artery into its internal and external branches. Note the completely organized thrombosis.

The right common carotid artery was exposed, as well as the internal and external branches. The vessels were of normal size. The internal jugular vein was also normal in size. The common carotid artery did not pulsate and had the consistency of rubber. An 18 gage needle introduced into the common carotid artery did not yield blood, nor could saline solution be introduced into the vessel. This abnormality was present in both the internal and the external branch of the common carotid artery.

The patient was readmitted to the hospital on Feb. 7, 1949, because of an episode of syncope associated with "shaking," in the course of which he had bitten his tongue.

An electroencephalogram at this time revealed focal voltage suppression in the right occipital area. There was no associated delta activity. On March 18, the right side of the neck was reexplored, and a segment of common carotid artery, including the bifurcation and short segments of the external and internal branches, was removed. Microscopic examination revealed thrombosis of the common, internal and external carotid arteries (fig. 2).

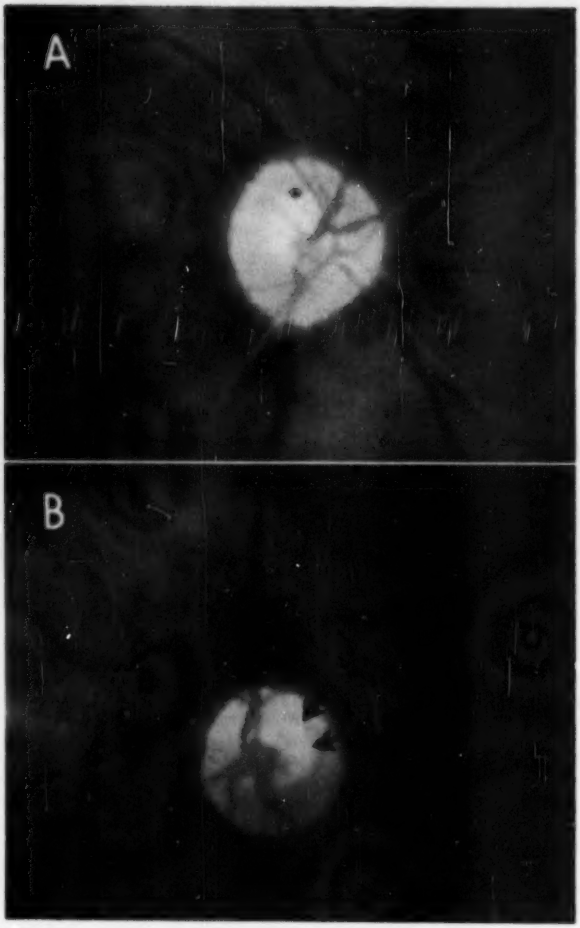

Fig. 3 (case 2).—Photographs (copied from kodachromes®) of the normal right disk (*A*) and the atrophic left disk (*B*). The arrows point to the zone of greatest pallor of the nerve tissue.

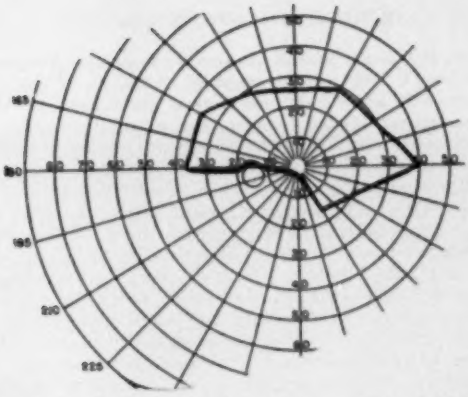

Fig. 4 (case 2).—Visual field of the left eye taken with the 5/330 white test object on Dec. 8, 1948 in a case of partial optic nerve atrophy associated with thrombosis of the carotid artery. Vision in this eye was 20/25 with correction.

Fig. 5 (case 2).—Photomicrograph showing the organized thrombosis of the common carotid artery. The vessel wall shows atherosclerotic changes.

Case 2.—C. B., a Negro aged 63, was admitted to the City of Detroit Receiving Hospital on Dec. 1, 1948, with the complaint of blurring of vision, which had become progressively worse during the previous four months. The blurring was greater in the right eye. He had also noted twitching of the left side of the face for approximately four months. His past history indicated that he had had hypertensive vascular disease for 15 years, with several episodes of mild cardiac decompensation. He had formerly been employed as a Pullman porter.

The patient was obese, weighing approximately 250 pounds (113.4 Kg.). There was twitching of the muscles about the left eye and cheek with increased pigmentation of that side of the face. The right optic disk was normal in color, with normal cupping (fig. 3 *A*). The veins were dilated, the artery-vein ratio being 2:3, with slight arteriovenous compression. No hemorrhages were noted. The macular area exhibited granular changes. The left optic disk was pale, with a moderate degree of cupping (fig. 3 *B*). The vessels, retina and macula were similar to those in the right eye. The right eye revealed normal peripheral fields with some enlargement of the blindspot. The left eye showed definite loss of most of the inferior field with contraction of the superior field (fig. 4). There was absence of the pulsations of the carotid artery in the left side of the neck. An electrocardiogram revealed sinus rhythm with left axis deviation and damage to the left ventricle. Roentgenologic studies of the chest showed considerable hypertrophy of the left ventricle. All other laboratory findings were normal. The electroencephalogram was essentially normal.

Exposure of the carotid artery and its component branches was made with the patient under general anesthesia. The jugular vein was observed to be enlarged to twice its normal size. The common carotid artery was firm and nonpulsatile throughout its extent, the vessel having been well exposed through its course in the neck. The thrombosed branches of the artery were likewise exposed and palpated as far as possible to the base of the skull. A needle inserted into the vessels showed no evidence of returning blood. A section of the artery 2 cm. in length was excised, and the ends of the artery were ligated. Microscopic examination showed pronounced atheromatous changes with organized thrombus occluding the lumen (fig. 5).

Case 3.—J. D. J., a Negro aged 26, was admitted to the City of Detroit Receiving Hospital on Nov. 2, 1949, with a history of having been in relatively good health until four weeks prior to admission, when he had abdominal pain and vomiting. One day prior to admission he had a "falling out" spell, with a burning sensation in the left side of his face. He gave no history of injury or previous vascular disturbances.

Examination revealed complete left hemiplegia and hemianesthesia with involvement of the fifth, seventh, eighth, ninth, tenth, eleventh and twelfth cranial nerves on the left and partial paralysis of the third nerve on the right. One day after admission, there developed thrombosis of the right central retinal artery with ptosis of the right upper eyelid. The blood pressure was 120/60. A diagnosis of thrombosis of the right common carotid artery was made.

An angiogram showed thrombosis of the right internal carotid artery just distal to the bifurcation. An electroencephalogram revealed pronounced voltage suppression in the right frontal and motor area with delta waves of moderate voltage from the right frontal pole. The patient's spinal fluid was clear and under normal pressure. Serologic reactions of the spinal fluid and blood were normal.

In March 1950, the patient was admitted to the Veterans Administration Hospital, Dearborn, Mich. Examination showed persisting left hemiplegia, complete atrophy of the right optic nerve and narrowing of the arteries in both fundi, the last being more marked on the right (fig. 6). The right pupil did not react to direct

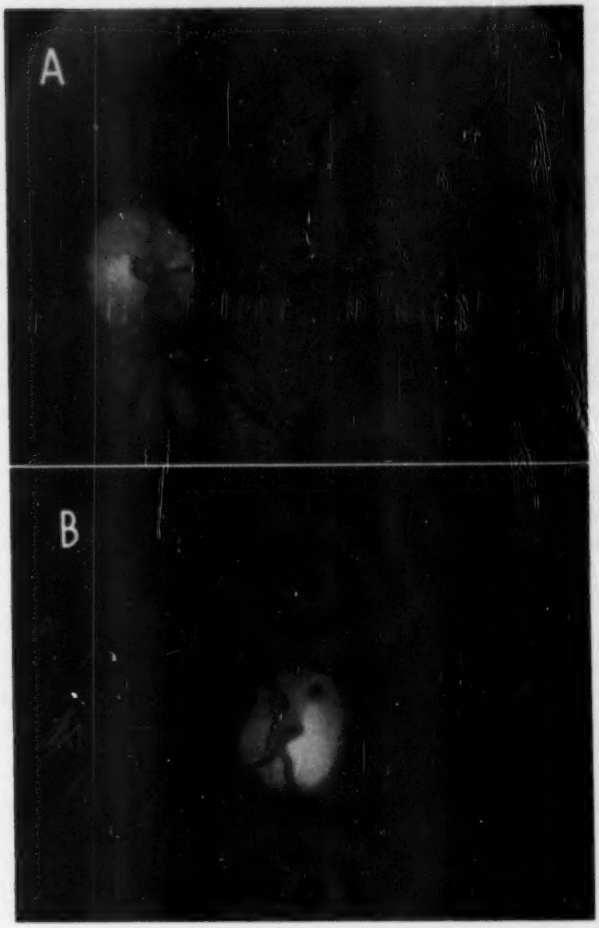

Fig. 6 (case 3).—Photographs (copied from kodachromes®) of the normal left disk (*A*) and the atrophic right disk (*B*).

stimulation with light. The visual acuity and visual field were unimpaired in the left eye. Examination otherwise gave essentially the same results as on the previous occasion.

On March 31, 1950, the internal carotid artery was exposed. It was ligated at both its distal and its proximal end and the portion between excised.

COMMENT

The three cases presented are instances of optic nerve atrophy, two complete and one partial, associated with thrombosis of the carotid arteries. The optic nerve atrophy in the cases in which there was unilateral blindness was due to occlusion of the central artery of the retina. In the third case the condition was not associated with any disturbance in the central artery. The two types of involvement of the optic nerve suggest two entirely different causes—the first, secondary to occlusion of the central artery, being the more obvious. The reasons for ocular involvement in these cases may be briefly considered.

It is well known that ligation of the main arterial trunk which supplies the eye, the internal carotid artery, does not cause blindness in nonarteriosclerotic persons. Obviously, the collateral circulation in such eyes is adequate. In persons with arteriosclerosis, the compensatory changes necessary for the development of collateral circulation are insufficient. In addition, it is likely that similar sclerotic changes involve the communicating arteries. Slowing of the blood flow also tends to favor thrombosis. Occlusion of the central artery may result from continuation of the thrombotic process along the main vessel or from sclerotic changes within its own walls, aided by the slowing of the blood flow.

Partial atrophy of the nerve is not due to any changes in the central retinal artery but is the result of involvement of the nutrient arteries of the optic nerve itself. The sclerotic process affecting these vessels, together with slowing of the blood flow, produces a "spotty" involvement of the optic nerve. This accounts for the irregularity of the visual field in such cases.

SUMMARY

Three cases of optic nerve atrophy, two complete and one incomplete, associated with thrombosis of the carotid arteries, are presented. The relation between the sclerotic process and the optic nerve atrophy is discussed.

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AMINO ACID COMPOSITION OF TISSUE PROTEINS OF THE CORNEA, SCLERA, VITREOUS AND RETINA

ALEXANDER J. SCHAEFFER, M.D.
AND
JOHN D. MURRAY
LOS ANGELES

A HISTORICAL survey of the available information on the biochemistry of the eye in Krause's monograph[1] shows a slow, progressive evolution. This knowledge concerning the protein chemistry of the cornea is relatively poor, and the information of earlier authors is of little value, as they are dated prior to the era of the protein chemistry opened by Fischer's ester method.

Quantitatively, the corneal tissue consists chiefly of the substantia propria, and, logically, most attention was given to that part. One of the earlier investigators, Müller,[2] found that it consists basically of collagen. Because of its physical characteristics, the protein reminded him of the basic substance of the cartilage, and he called it chondrogen. The investigations of Bruns,[2] His,[2] Fubini [2] and Morochowetz [2] moved on a similar plane, until Mörner [3] offered more definite details. He found that the corneal tissue contains mainly collagen, with a smaller quantity of mucoid.

The first amino acid analysis of the proteins of the corneal tissues was attempted by Jess.[4] This investigator did not isolate the individual proteins of the cornea; he made his estimations on the total proteins, hydrolyzing the whole tissue. His determination involved three amino acids—histidine, arginine and lysine. Since these determinations were

1. Krause, A. C.: The Biochemistry of the Eye, Monograph no. 2, Wilmer Ophthalmological Institute, Johns Hopkins Hospital and University, Baltimore, Johns Hopkins Press, 1934.

2. Cited by Krause.[1]

3. Mörner, C. T.: Untersuchungen der Proteinsubstanzen in den lichtbrechenden Medien des Auges: II., Ztschr. f. physiol. Chem. **18**:213, III., 233, 1894.

4. Jess, A.: Zur vergleichenden Chemie der Hornhaut und der Lederhaut des Auges, Arch. f. Ophth. **112**:489, 1923.

made on the undivided, whole proteins, his results are comparable only with those of Schaeffer and Shankman.[5]

The investigations of Krause[6] signify a turning point in this line of research. He showed the quantitative presence of three insoluble proteins in the substantia propria of the cornea and in the sclera, namely, mucoid, collagen (or gelatin) and elastin, and estimated their contents in arginine, histidine, lysine, cystine, tryptophan and tyrosine.

Already the earlier investigators had attempted the division of the corneal tissue into its components for further analysis. Essential data on the epithelium were furnished by Krause, who found that it contained 80.47 per cent water and 19.53 per cent solids. Of the solids, 42.10 per cent is an insoluble protein, while of the soluble aqueous extract, 31.20 per cent is soluble protein, all but 0.7 per cent of which is noncoagulable. The endothelium on chemical analysis is found to be basically similar to the epithelium.

Schaeffer and Shankman[5] estimated the amino acid constitution of the total corneal proteins by the microbiological assay method, and they estimated 14 amino acids.

The history of the protein chemistry of the sclera is very similar to that of the cornea. Mörner found 87 per cent collagen and 13 per cent mucoid and overlooked elastin completely. Jess made his amino acid determinations on the whole scleral substance; his analysis involved, as in the case of the cornea, histidine, arginine and lysine.

In Krause's analysis, the bovine sclera contained 27.76 per cent solids, of which 27.06 per cent was organic matter containing (of the total fresh substance) 2.31 per cent mucoid, 22.14 per cent collagen, 1.45 per cent elastin and little albumin, globulin, nucleoprotein or water-soluble extracts. As in the case of the cornea, his analysis involved the determination of arginine, histidine, lysine, cystine, tryptophan and tyrosine, in the mucoid, collagen and elastin.

Schaeffer and Shankman, in their preliminary investigation, made amino acid determinations of the whole proteins of the sclera; thus, their results can be compared with the results of Jess only, and no comparison with those of Krause is admissible. As in the case of the cornea, the total protein of the sclera was investigated as to its amino acid content by the microbiological assay method, and here, again, 14 amino acids were estimated.

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5. Schaeffer, A. J., and Shankman, S.: Amino Acid Composition of Proteins of the Ocular Tissues, Am. J. Ophth. **33**:1049, 1950.

6. Krause, A. C.: The Chemical Constitution of the Cornea, Am. J. Ophth. **15**:422, 1932; Die chemische Zusammensetzung der Eiweisse in der Hornhaut, Arch. f. Augenh. **107**:453, 1933; The Chemical Constitution of the Sclera, Arch. Ophth. **7**:598 (April) 1932; The Chemistry of the Sclera, Am. J. Ophth. **16**:214, 1933.

One interesting deduction was made by Schaeffer and Shankman from the amino acid values obtained for the total proteins of the cornea and sclera. The three amino acids, arginine, histidine and lysine, were found in a proportion similar to that in the eukeratins. Eukeratin is defined as an insoluble protein, resistant to enzymatic digestion, and yielding histidine, lysine and arginine in a molecular ratio of approximately 1 : 4 : 12. This keratin has been found principally in hair of human beings, cows, camels and chimpanzees; in finger nails; in cattle horn, etc. According to the findings of these authors, the cornea and the sclera might be considered keratinoid in composition. Of course, such consideration would be admissible only in case this ratio of the three amino acids is demonstrated in the insoluble protein fraction of these tissues also. A further investigation of the amino acid composition of the individual proteins was therefore of the utmost interest. They determined also a high aminoacetic acid (glycine) content of the cornea and the sclera. Some differences were found between the composition of the sclera and that of the cornea, namely, leucine, isoleucine and phenylalanine, which may possibly be significant, but this could not be claimed on the basis of the limited data.

In a previous paper we [7] reported on the amino acid composition of the individual proteins in bovine crystalline lenses. In connection with those analytical studies, we have now investigated the amino acid composition of the total, as well as the isolated individual, proteins in several tissues of the bovine eye, using the same microbiological assay method as in the previous study. Thus, the present paper has the purpose of completing the data concerning the chemical composition of the tissue proteins of the eye. A general survey of all available data will reveal the fact that, while the basic knowledge on this problem has been enlarged in the last few years, many lacunas have yet to be filled. The recent advancements in the field of protein research, especially the microbiological assay method and partition chromatography, are furnishing valuable analytical tools which facilitate the investigation, and further advances are to be expected in the near future.

It is obvious that analysis of the undivided tissue gives no hint as to the chemical characteristics of a tissue type. Similarly, the analysis of the undivided proteins does not reveal the chemical composition of a specific protein molecule in the cell structure. The crystalline lens represents a histologically homogeneous tissue, whereas the other ocular tissues are relatively complex structures and, besides their proper cell elements, contain nerve elements and often blood vessels, lymphatics, etc. Evidently, the distribution of proteins and their amino acid composition vary with the morphological variability of the cell elements. In the

7. Schaeffer, A. J., and Murray, J. D.: Amino Acid Composition of the Lens Proteins of the Bovine Eye, Arch. Ophth. **43**:1056 (June) 1950.

sclera, though lymphatics are missing, the nerve and blood supply are complicating features in the cellular architecture, which appears to be anything but homogeneous. The presence of chromatophores in the lamina fusca signifies not only a histological, but evidently a chemical, factor in the tissue complex. The same may be said of the cornea as a whole. Though its separated layers possess a greater homogeneity, the presence of nerve elements in the substantia propria is a complicating fact. The authors did not attempt the investigation of Bowman's and Descemet's membranes, as the isolation of these structures requires particular technic and attention.

METHODS OF INVESTIGATION [8]

To achieve results which would also allow comparison with analytical data of previous investigators, we estimated the amino acid composition of the cornea and sclera (and, tentatively, of the vitreous and the total retina) by the microbiological assay method. This method has already been described in connection with our investigation of the protein composition of the crystalline lens. In the present research the different tissues or isolated proteins were hydrolyzed in the following order:

Undivided, total proteins	Divided, individual proteins of the corneal stroma and of the scleral tissue
1. Total sclera	1. Mucoid
2. Total corneal stroma	2. Collagen
3. Corneal epithelium	3. Elastin
4. Total vitreous humor	
5. Total retinal tissue	

The method for the separation and isolation of the individual proteins followed in the main the technic described by Krause and consisted principally of the following procedures:

Corneal Stroma.—Stromas of 13 bovine eyes were macerated and extracted five times with distilled water at 4 C. No coagula were obtained from this extract.

Mucoid: The residue was extracted four times with one-half saturated lime water (solution of calcium oxide) by letting it stand 12 hours at 4 C. each time. The extracts were combined, and 1 per cent acetic acid was added for maximum precipitation. This precipitate was centrifuged and washed with water. The solid was then redissolved in lime water and reprecipitated by addition of acetic acid. Finally, it was washed with water, alcohol and ether and dried *in vacuo*.

The residue from the mucoid was washed four times with water, four times with 0.1 per cent acetic acid and four times with water.

Collagen: The residue was extracted with distilled water at 95 C. for six hours, then three times more for two hours per extraction. The combined water extracts were evaporated until viscous, centrifuged until they were clear and then poured into 200 ml. of absolute alcohol U. S. P. To the cloudy solution was

8. The H. M. Chemical Laboratories, Los Angeles, permitted use of their facilities and rendered technical assistance.

added 250 ml. of ether to precipitate the collagen. This was centrifuged, washed with alcohol and then redissolved in water and precipitated as before. Finally, the collagen was washed with alcohol and ether and dried *in vacuo*.

Elastin: The residue from collagen was centrifuged and washed with alcohol and ether.

Sclera.—The procedure for the sclera was the same as that for the corneal stroma.

The water extract yielded coagula at 50 to 57 C., 61 to 64 C. and 72 to 85 C. The amounts obtained were too small for analysis.

The percentage contents of the individual proteins of the tissue fractions examined were found to be as follows:

	Corneal Stroma, %	Sclera, %
Mucoid	16.35	10.70
Collagen	78.50	79.00
Elastin	2.50	7.00

Comment.—The mucoid of the cornea and the sclera is classified as a glycoprotein. The glycoproteins are conjugated proteins which contain the protein molecule united to some molecule or molecules other than a salt. They are compounds of the protein molecule with a substance containing the carbohydrate group other than a nucleic acid. The mucoid itself is an ester of the protein and of mucoitin sulfuric acid, as its prosthetic group. On hydrolysis this yields sulfuric acid, acetic acid, hexuronic (as corlic) acid and a hexosamine. It is very likely that the combination of the carbohydrate and the protein takes place as in other peptic linkages.

The collagen is the largest protein portion of the corneal stroma and of the sclera. On hydrolysis collagen is changed to gelatin, particularly on prolonged heating. The collagen of the sclera and corneal stroma are obviously very similar to collagens of other tissues, such as connective tissue and cartilage, though greater differences are recognized. Krause suggested that more than one collagen is present at once in the same tissues. There is a quantitative variability in collagen depending on the age, as tissues of younger animals seem to contain more water and mucoid and less collagen than those of older animals. It is very likely that the content and composition of the collagen vary with species, and perhaps also with sex.

The third major protein of these tissues is elastin, an albuminoid present in elastic tissues, usually in ligaments but also in walls of arteries; it is the principal component of the yellow elastic tissue.

It is likely that these major components of the corneal (stroma) and scleral tissue proteins are the same as those of connective tissues of the cartilage, though small quantitative variations are the determining factors of the characteristics in each of these tissue forms.

Albumin and globulin were not investigated, since sufficient amounts were not obtained.

Besides these tissues, we have investigated the amino acid distribution in three other structures, viz., the corneal epithelium, the vitreous humor and the total proteins of the retina. These were hydrolysed *in toto*. Table 3 summarizes the findings obtained.

RESULTS

The results of these investigations are summarized in two tables. Table 1 shows the amino acid distribution in the total proteins of the examined tissues. Table 2 gives the amino acid values in the divided, individual proteins. In both tables, for reasons of comparison, the data

TABLE 1.—*Amino Acid Distribution, Expressed as Percentage, in the Undivided, Total Proteins of Cornea and Sclera*

	Cornea, %			Sclera, %		
Amino Acids	Jess	Schaeffer and Shankman	Present Investigation	Jess	Schaeffer and Shankman	Present Investigation
Aminoacetic acid (glycine)	....	18.0	....	....*	17.5	....
Valine	....	3.8	3.9	....	3.7	3.6
Leucine	....	4.7	5.4	....	4.0	5.0
Isoleucine	....	2.0	3.2	....	2.4	2.4
Phenylalanine	....	2.9	2.9	....	2.3	2.4
Tyrosine	....	1.4	1.6	....	1.3	1.5
Tryptophan	....	....	0.4	....	....	0.4
Glutamic acid	....	11.0	11.2	....	10.8	10.9
Aspartic acid	....	7.4	7.4	....	6.6	6.3
Cystine	....	....	0.9	....	....	1.1
Methionine	....	1.1	1.8	....	1.2	1.9
Arginine	5.51	7.0	7.8	2.90	7.6	8.8
Histidine	0.39	0.7	1.0	0.78	0.8	1.1
Lysine	5.52	3.8	4.4	11.56	3.6	5.7
Threonine	....	2.9	3.6	....	2.7	3.7
Total	12.02	68.2	65.5	15.24	64.7	64.8

of earlier authors are also incorporated, namely, those of Jess and Krause, respectively.

The values obtained in our investigation and those of Krause and of Schaeffer and Shankman are in close agreement. The small, or sometimes appreciable, differences in results gained by chemical method and by the microbiological assay method might be explained by the limitations of both methods, and only further investigation with independent analytical methods will make the already existing agreement a closer one.

Data on the undivided, total proteins of the sclera and cornea were furnished by Schaeffer and Shankman, as well as by the present study. In both investigations 14 amino acids were estimated, of which 12 were for the same substances; thus, on summary of the results, data on 16 amino acids are available, besides the three values of Jess for arginine, histidine and lysine.

The data missing in the study by Schaeffer and Shankman for tryptophan and cystine are furnished in the present investigation, and those for aminoacetic acid and serine, which we did not estimate, are given by Schaeffer and Shankman. No data at all are available for alanine, proline, hydroxyproline and citrulline.

The main feature in our findings is the low total value of amino acids for the corneal stroma and for the sclera, which was found to be approximately 50 per cent. Corresponding values obtained by Schaeffer and Shankman amounted to 72.5 per cent for the cornea (total tissue) and

TABLE 2.—*Amino Acid Distribution, Expressed as Percentage, in the Divided, Individual Proteins of the Cornea and Sclera (Collagen, Elastin and Mucoid)*

	Cornea						Sclera					
	Collagen		Elastin		Mucoid		Collagen		Elastin		Mucoid	
Amino Acids	Krause	Present Investigation	Krause	Present Investigation	Krause	Present Investigation	Krause	Present Investigation	Krause	Present Investigation	Krause	Present Investigation
Valine	.....	3.2	.....	3.3	.....	3.9	.....	3.26	.....	3.8	.....	6.3
Leucine	.....	4.4	.....	4.85	.....	7.6	.....	4.2	.....	6.1	.....	9.6
Isoleucine	.....	2.04	.....	2.9	.....	5.8	.....	2.06	.....	2.56	.....	4.5
Phenylalanine	.....	2.4	.....	2.7	.....	4.1	.....	2.1	.....	2.77	.....	4.2
Tyrosine	1.05	1.1	2.99	2.75	3.64	3.26	0.9	0.85	2.35	2.22	6.17	5.3
Tryptophan	0.004	0.24	0.32	1.12	1.04	1.05	0.07	0.22	0.22	1.05	0.75	1.4
Glutamic acid	.....	10.8	.....	12.05	.....	11.2	.....	10.6	.....	11.2	.....	11.5
Aspartic acid	.....	7.05	.....	7.8	.....	8.5	.....	5.7	.....	6.55	.....	7.6
Cystine	0.6	0.66	1.57	1.26	4.37	4.04	0.67	0.91	0	0.42	2.11	1.94
Methionine	.....	1.1	.....	2.4	.....	7.9	.....	1.75	.....	1.95	.....	3.5
Arginine	8.01	8.6	6.04	7.25	5.86	6.55	8.33	8.4	10.56	9.24	11.12	9.06
Histidine	2.62	0.85	5.55	2.7	2.12	1.02	2.96	1.3	0.23	0.45	1.39	0.85
Lysine	4.91	4.32	2.98	3.2	2.2	4.4	6.38	5.7	0.74	4.2	3.3	3.7
Threonine	.....	2.02	.....	2.56	.....	3.6	.....	2.72	.....	3.3	.....	9.4
Total	17.284	50.38	19.45	57.54	20.23	80.52	19.31	58.78	19.10	56.80	34.65	78.84

68.5 per cent for the sclera. This difference in the values is in part explained by the high aminoacetic acid content evidenced in the analysis of Schaeffer and Shankman, which was not included in our investigation.

The estimation of the divided, individual proteins, of course, offers more valuable information.

As the tables show, the total values for collagen in the corneal stroma and in the sclera are only close to 50 per cent of the total protein value; thus, it is expected that the missing amount is contained in the amino acids not yet analyzed, i. e., in aminoacetic acid, alanine, proline, hydroxyproline and citrulline. The last amino acid is expected to exist only in very small amount in these tissues or to be missing entirely, as its presence has not yet been shown in similar tissue proteins. Rather, it is to be expected that high values for aminoacetic acid, proline and hydroxyproline will be found.

For the mucoid of the cornea and the sclera, the total value of the determined amino acids amounts to something over 75 per cent; thus, the value of the missing six amino acids is relatively low. An aminoacetic acid content of 18 per cent for the total corneal proteins and of 17.5 per cent for the sclera was found by Schaeffer and Shankman. It remains to be determined how much of this amount is distributed in the mucoid alone, as it will necessarily be lower than in the other two proteins. Characteristic of the mucoid is also its higher content in tyrosine, phenylalanine, lysine, leucine, isoleucine, methionine, cystine, asparagine and valine. As its glutamic acid content is not considerably higher than that of the other two proteins, it is expected that its proline and

TABLE 3.—*Amino Acid Distribution, Expressed as Percentage, of the Tissue Proteins in the Corneal Epithelium, Vitreous and Retina*

Amino Acids	Corneal Epithelium, %	Vitreous, %	Retina, %
Valine	6.6	5.5	6.2
Leucine	10.1	8.4	6.9
Isoleucine	6.4	4.4	4.3
Phenylalanine	4.9	5.0	1.7
Tyrosine	2.6	2.4	1.6
Tryptophan	2.6	2.4	2.1
Glutamic acid	15.2	13.2	8.1
Aspartic acid	8.5	8.4	trace
Cystine	2.1	0.9	2.3
Methionine	4.0	0.9	1.6
Arginine	6.9	5.6	10.4
Histidine	2.1	2.5	2.2
Lysine	7.1	6.1	5.8
Threonine	5.0	6.6	6.8
Total	85.7	73.6	59.8

hydroxyproline contents will be relatively low. The mucoid of the corneal stroma and that of the sclera also show appreciable differences. The sclera contains more histidine, tyrosine, lysine and leucine, whereas the stromal mucoid is richer in isoleucine, methionine, cystine and tryptophan.

The collagen, as already mentioned, is expected to be rich in aminoacetic acid, proline and hydroxyproline. The total value of the determined amino acids is below that found for elastin. It is generally poorer in most of the determined amino acids than is elastin.

After separation of the three individual proteins, the suspected characteristic proportion of histidine, lysine and arginine, in approximately a molecular ratio of 1:4:12, disappears, and the supposition that the corneal and scleral tissues contain proteins which are essentially keratinoid in nature cannot be confirmed.

As mentioned above, we have also tentatively determined the amino acid content of the total proteins of the corneal epithelium, the vitreous humor and the undivided, total retinal tissue (table 3). These estimates

necessarily have only restricted values, since the various proteins have not been isolated. Particularly, the retina represents a highly complex tissue, and values obtained after hydrolysis of the total tissue cannot give any information for chemical constitution of any of its cell elements. On the other hand, this procedure might be valuable in general physiological investigations, especially in nutritional research. More informative are the data on the corneal epithelium and on the vitreous, structures which are more uniform and homogeneous.

SUMMARY

The amino acid composition of the total proteins in the corneal stroma, sclera, corneal epithelium, vitreous humor and retinal tissue of the bovine eye was determined by the microbiological assay method. In further study, the individual proteins of the corneal stroma and of the sclera were isolated, and the amino acid composition of these proteins—mucoid, collagen and elastin—was estimated by the same method. The values obtained were tabulated and compared with the results of other investigators.

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OPHTHALMIC SYMPTOMS IN GIANT FOLLICULAR LYMPHADENOPATHY

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BRILL, Baehr and Rosenthal[1] (1925) described a syndrome that is characterized by follicular hyperplasia of the lymph nodes, often accompanied with splenomegaly, and remarkably remediable with roentgen irradiation. It has been accepted generally as a specific disease. Numerous case reports and several monographs have dealt with it. Symmers (1938)[2] published the first large paper, and the disease is often called the Brill-Symmers syndrome. The usual terms in the United States literature are "follicular lymphoblastoma" and "giant follicular lymphadenopathy." The disorder is fairly well defined, and after histological examination of a lymph node the diagnosis is usually easy. The number and size of the follicles are increased; the cellular tissue is composed of comparatively large cells with numerous mitoses and tends to invade the fibrous capsule; often the entire lymphadenoid system is involved, but sometimes certain groups of glands only are affected; usually the blood picture is completely normal except for inconstant eosinophilia and a measure of relative lymphocytosis. The disease is remarkably chronic, and cases under observation for more than 10 years have been reported. The general physical condition is usually not affected. Cure is apparently spontaneous in some cases, but cases of a malignant form, ending in cachexia and anemia, occur; sometimes the condition progresses to lymphosarcoma,[3] a fact which supports the view that giant follicular

From the Department of Ophthalmology (Chief, Dr. A. Samuelson), Central Hospital.

1. Brill, N. E.; Baehr, G., and Rosenthal, N.: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, J. A. M. A. **84**:668 (Feb. 28) 1925.

2. Symmers, D.: Giant Follicular Lymphadenopathy With or Without Splenomegaly: Its Transformation into Polymorphous Cell Sarcoma of the Lymph Follicles and Its Association with Hodgkin's Disease, Lymphatic Leukemia and an Apparently Unique Disease of the Lymph Nodes and Spleen—A Disease Entity Believed Heretofore Undescribed, Arch. Path. **26**:603 (Sept.) 1938.

3. Symmers.[2] Rubenfeld, S.: The Radiation Treatment of Giant Follicular Lymphadenopathy and Its Polymorphous Cell Sarcoma Derivative (Symmers' Disease), Am. J. Roentgenol. **44**:875, 1940. Brück, C.: Fall av Symmers sjukdom, Nord. med. **17**:505, 1943.

lymphadenopathy is a precursor of the latter disorder. Some factors, however, suggest that giant follicular lymphadenopathy may be caused by infection. Various disorders of the skin have often preceded or accompanied the disease,[4] and chronic lymphadenitis which has its onset with such diseases has been said to be prodromal to fully developed giant follicular lymphadenopathy. Braley and Alexander[5] (1947) were able to cultivate virus from lymph nodes which perhaps were affected with giant follicular lymphadenopathy.

Only the lymph nodes and the spleen have exhibited pathological changes in most of the cases that have so far been described. The disease has consequently manifested itself chiefly as local symptoms from these organs, and perhaps also as pressure due to their enlargement (ascites; hydrothorax). As long ago as 1931, however, Baehr, Klemperer and Rosenthal[6] stated that the lymphoid tissue tends to invade other organs also, e. g., the lacrimal glands, with resulting exophthalmos. The latter observation brings the disease within the ophthalmologist's sphere of interest, particularly as in the initial stages the ophthalmic symptoms seem to be the only ones. Very few such cases have been described. I feel justified, therefore, in giving the particulars of a case of giant follicular lymphadenopathy in a patient admitted to the ophthalmologic clinic at Gävle, especially since the clinical picture was rather singular.

REPORT OF A CASE

N. B., a factory worker, born in 1900, had previously been healthy on the whole, with no noteworthy illnesses except alleged attacks of pneumonia at the ages of 14 and 18. He denied having had venereal disease.

In the summer of 1946 the patient discovered some soft lumps at the angles of the jaw and on the neck; these gradually increased in size and number. At the same time he had itching of the skin, but the symptom vanished fairly soon. In November he was admitted to the medical clinic at the Central Hospital, Gävle, where generalized lymphadenoid hyperplasia was found. The lymph nodes were palpable in both cubital fossae, as well as over the left scapula; the spleen was not palpable. The sedimentation rate of the blood was 30 to 40 mm. in one hour, the eosinophils were slightly increased (4 to 9 per cent). The Wassermann test was ineffective, owing to inhibition of complement; the Kahn test gave a strongly positive reaction, but the reactions to the Müller and Meinicke tests were negative; the reaction was considered nonspecific. A lymph node was excised for biopsy. Its cellular arrangement was fairly homogenous, with rounded, atypical cells and many mitotic nuclei,

4. Combes, F. D., and Bluefarb, S. M.: Giant Follicular Lymphadenopathy: Association of Giant Follicular Lymphadenophy and Its Polymorphous Cell Sarcoma Derivative, Symmers' Disease, with Lesions of Skin, Arch. Dermat. & Syph. **44**:409 (Sept.) 1941. Brück, C.: Symmers' disease, Acta dermat-venereol. **25**:411, 1945.

5. Braley, A. E., and Alexander, R. C.: Virus Studies in Lymphomatoid Diseases of the Ocular Adnexa, Am. J. Ophth. **30**:1369 (Nov.) 1947.

6. Baehr, G.; Klemperer, P., and Rosenthal, N.: Follicular Lymphoblastoma, Am. J. Path. **7**:558, 1931.

and stains for stroma showed an intercellular reticulum. With some hesitation, the condition was diagnosed as reticulocellular sarcoma. It was remarkable, though, that the patient was in good condition; nor was there anemia of any kind. The patient had been fully able to work, without difficulty.

A series of roentgen treatments was given, the lymph nodes decreasing somewhat after comparatively small doses (200 r). The same therapy was given in April and July 1947.

In the spring of 1948 the patient began to have nasal symptoms, and roentgenologic examination revealed involvement of the ethmoid and maxillary sinuses. Deviation of the nasal septum being present, septal resection was considered but was thought inadvisable, owing to the poor prognostic significance of the lymphadenopathy. The sedimentation rate was then between 90 and 100 mm. in one hour.

Roentgen radiation was again given to the lymph nodes in April 1948. At approximately the same time the patient noticed that his eyelids began to swell, a symptom which became increasingly prominent in the autumn of the same year. At the turn of the year an impetiginoid eruption broke out on the skin around the wrists and over the cheeks and neck. The physical condition was satisfactory except for a slight leanness, but the patient had lost no weight in the preceding years. On Jan. 7, 1949 the patient was admitted to the ophthalmologic clinic, exhibiting the following picture:

The visual acuity was just below 1.0 bilaterally and the eyes were emmetropic. The eyelids were slightly swollen on both sides. The upper and lower fornices of the right eye and the upper fornix of the left eye contained protruding, bluish red, abundantly vascularized, soft tumorous growths, the largest of which was the size of half an almond. Staining with rose bengal revealed numerous spots in the rimal region of the bulbar conjunctiva of the left eye, as well as some on the cornea, whereas the right eye was not stained. The interior of both eyes was normal. At this time, also, there was no anemia, but the blood contained 14 per cent eosinophils, as well as a certain increase in immature leukocytes. A specimen obtained by sternal puncture showed normal cellular structure. The Wassermann test was complement inhibitory, and the other tests for syphilis, including Kahn's, gave negative results. As before, the sedimentation rate was 90 mm. in one hour. Large numbers of enlarged lymph nodes were palpated in the same areas as before. In addition, roentgenographic studies showed hilar lymphomas and great enlargement of the spleen, so that its lower pole extended a few centimeters beyond the iliac crest. Veiling and mucosal swelling were still visualized in roentgenograms of the paranasal sinuses.

Since it was thought strange that the physical condition was still entirely unaffected, more than two years after the diagnosis of reticulocellular sarcoma had been made, a lymph node was again excised, which, together with some of the tumor at the site of the palpebral part of the left lacrimal gland, was subjected to biopsy by Prof. N. Gellerstedt, Uppsala. His report follows. "Lymphoid proliferation with follicles extends throughout the parenchyma but leaves some sinuses intact. The follicles, however, are not of the usual mature type, with reactive foci. Although they have irregular nuclei, the cells on the whole resemble lymphocytes. In the form of diffuse knots, the same type of lymphoid tissue, but not with equally distinct follicular structures, has invaded and destroyed the lacrimal gland." The microscopic diagnosis was follicular lymphoblastomatosis (figs. 1 and 2).

At the end of January 1949, at the medical clinic, Uppsala, 2.5 millicuries of radioactive phosphorus (P^{32}) was given therapeutically. The lymph nodes, as well as the tumorous growths around the eyes, decreased notably with this treatment.

A check-up on the condition in the middle of April 1949 revealed increased subjective dryness of the eyes, greater stainability of the left eye with rose bengal and some stainable spots on the right cornea. The left cornea being extremely rugose, full visual acuity could not be attained with that eye (vision, 0.4). The

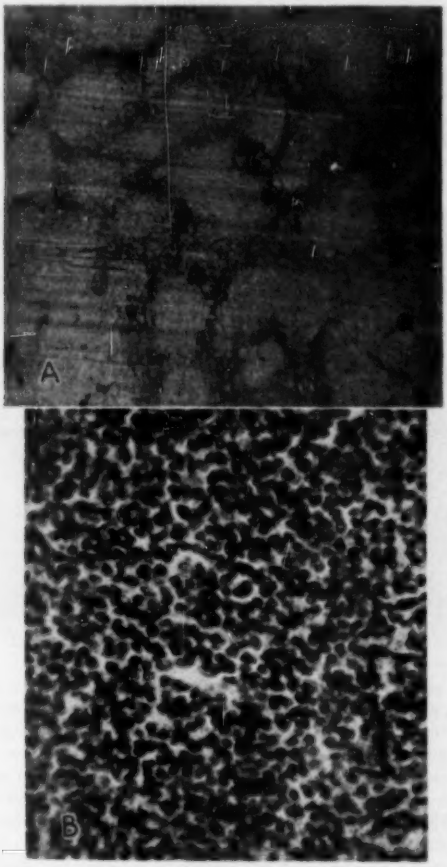

Fig. 1.—*A*, low power photomicrograph of lymph node. Azan stain. *B*, high power photomicrograph of lymph node.

patient complained also of dryness of the mouth. Conservative treatment of the ocular symptoms with eye drops was attempted, but the results were not satisfactory.

At the end of April 1949 the patient had an attack of typical herpes zoster, a region 10 cm. wide on the left lower part of the thorax being covered with efflorescences. Recovery was uneventful.

Owing to the persistent symptoms from the nose, which took the form chiefly of a sensation of occlusion of the nasal passages, septal resection was performed in June 1949 at the otorhinolaryngological clinic, Uppsala. The relief was slight and temporary.

The skin on the lower eyelid and at the nasal canthus on the right side began to swell and turn red in the middle of July 1949. The picture suggested phlegmonous dacryocystitis, but it was not quite characteristic in that the skin was remarkably cyanotic and on palpation appeared firmly infiltrated, thickened and scarcely movable against the underlying skeletal parts. A fistula developed. Temporary amelioration was achieved by conservative treatment, but after two weeks the symptoms returned with increased temperature, so an incision had to be made. Healing occurred soon, and the nasolacrimal duct, which up to then had been obstructed, was patent. A certain relative resistance to irrigation was felt, however. Two more exacerbations

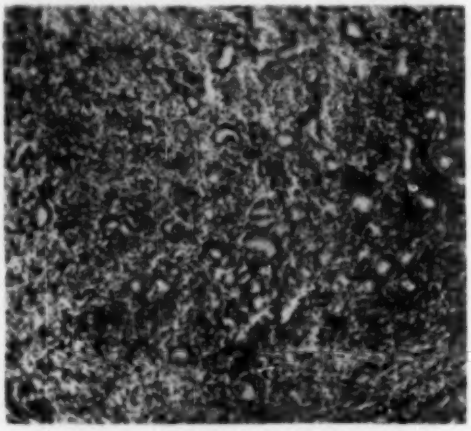

Fig. 2.—Lacrimal gland invaded and destroyed by lymphoid tissue.

occurred one and two months later, respectively. Thereafter the lacrimal duct was irrigated with penicillin for some time, and the condition improved enough to make possible dacryocystectomy, on Oct. 17, 1949. The lacrimal sac was very large, owing chiefly to a considerable, irregular thickening of its wall, which was remarkably fragile. Microscopic examination revealed that the wall of the sac was infiltrated with lymphoid tissue without reactive foci. Only small epithelial remnants were left (fig. 3). The process was considered the same as that seen in other preparations in this case (Prosector S. Ranström, Uppsala).

The slight symptoms of keratoconjunctivitis sicca that had been seen earlier in the patient's right eye disappeared at the same time that the repeated attacks of dacryocystitis put the lacrimal duct out of action. It was thought possible, therefore, that closure of the canaliculi, e. g., by diathermy, might effect improvement also on the left side. The operation was accordingly performed, and in 24 hours the distress was much relieved and the visual acuity again almost normal, the corneal surface having become smoother.

A complete medical examination in October 1949 showed that the regional lymph nodes were enlarged to approximately the same extent as before. A diffuse, granular infiltration, in addition, was palpable in the left cheek. Inspection of the pharynx showed that the tonsils were small and not pathological. In the nasopharynx, on the other hand, there was a mass, which was visible roentgenographically as well. Part of the lump was excised for biopsy, which revealed the following changes: "The true lymphoid tissue deviates slightly from normal in that the follicles are very large, are not sharply outlined and in part merge diffusely with the surrounding lymphoid parenchyma. The latter, like the follicles, is composed of fairly similar, equidimensional, rounded or polygonal cells with moderately chromatin-rich nuclei. The cells resemble those seen in the large follicles of a follicular lymphoma. There are very few mitoses, however, and the picture might equally well be that of chronic inflammatory changes in hyperplastic lymphadenoid tissue. The decision

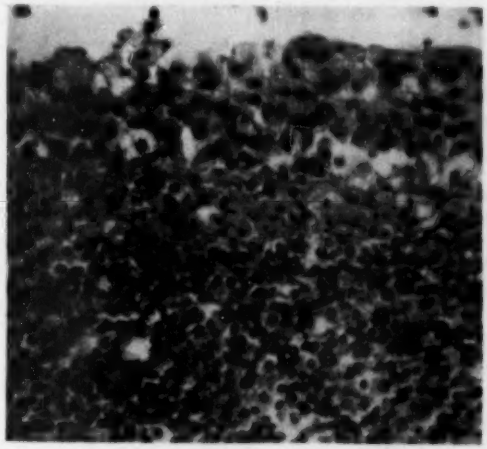

Fig. 3.—Infiltration of lymphoid tissue in the wall of the lacrimal sac.

cannot be made with certainty on the basis of the submitted sample." (Prof. O. Reuterwall, Stockholm.)

The tumorous growths in the superior and inferior conjunctival fornices of the right eye were extirpated also. It was noted that they were fairly easy to cut loose near the roots but were fused to the conjunctiva, which therefore was considerably involved. The tumors were bluish red, soft, almost spongy in consistency and invested with a very thin capsule. Microscopic examination disclosed tumorous tissue, fundamentally similar to that examined previously. In addition, a piece of the lacrimal gland was found infiltrated with the same tumor tissue.

The pathological changes in the composition of the blood proteins, which previously had been manifested as an increased sedimentation rate, were verified by repeated tests. Sedimentation rates exceeding 90 mm. in one hour were obtained, and on one occasion the rate was 121 mm. in one hour. Positive reactions for euglobulin and alkaside and to the Takata-Ara test were obtained also. The

"formol"-gel test produced a gel in serum within less than one minute. On one occasion electrophoretic analysis of the plasma was performed; it disclosed the presence of moderate hyperproteinemia, the increase consisting mainly of gamma globulin and fibrinogen. The values for albumin were simultaneously subnormal (total proteins, 9.8 Gm.; albumin, 3.2 Gm.; alpha globulin, 0.9 Gm.; beta globulin, 1.1 Gm.; gamma globulin, 3.2 Gm., and fibrinogen, 1.2 Gm., per 100 cc.). The tests for syphilis, which formerly had yielded undecisive results, were again made. The Wassermann test now showed zero hemolysis, and titration, from 0.2 to 0.0015 cc., did not change the strength. The reactions to the Kahn and Meinicke tests were considered positive (+++), as was that to Müller's test (++).

Under the assumption that the patient's condition might be due to infection, penicillin treatment was now tried. Up to 250,000 units was given four times daily for rather more than a week. There was no observable effect on the size of the lymph nodes, but the cutaneous manifestations receded. A new course of roentgen treatments with small doses (150 r on two occasions) made the nodes much smaller

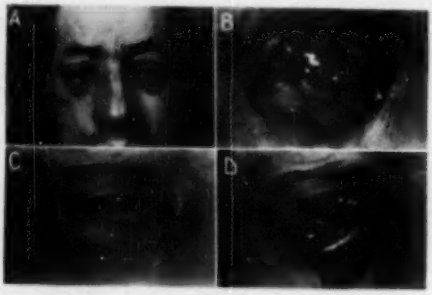

Fig. 4.—Patient in October 1949, 10 days after dacryocystectomy on the right side. The eyelids are swollen (*A*, *B*), due to tumorous growths in the upper (*C*) and lower (*D*) fornices. Infiltration appears in the left cheek (*A*).

also, and some disappeared altogether. Moreover, the infiltration of the left cheek became much less extensive.

At the end of December 1949 an exacerbation of the patient's skin disorder occurred. A number of efflorescences gradually developed on both hands. The condition resembled erythema multiforme exudativum. Simultaneously, the temperature increased slightly, but after a time it returned to normal. The symptoms vanished after about one month.

The swelling around the eyes having increased in the first part of February 1950, the patient was readmitted to the ophthalmologic clinic on Feb. 23, 1950. The right eye contained the only traces of the previous tumors in the fornices. There were prominent areas of resistance, however, around the left orbital opening; they were palpable through the eyelids, which when everted disclosed large tumorous growths in the upper and lower fornices. A granular infiltration, the size of a child's palm, was felt in the skin on the temporal side of the left orbit. Granular infiltrations of the same type as those previously present in the left cheek were now palpable in both cheeks. Similar masses were observed also in the upper and lower lips, close to the corners of the mouth. The roof of the mouth exhibited a few round, finger nail–sized elevations, which probably were of the same type. Practically all the

previously palpable lymph nodes had disappeared. However, two firm nodes, the size of a date stone, was still felt at each angle of the lower jaw, and so were a pair of cubital nodes of approximately the same size.

Two roentgen treatments with the same small doses resulted in almost complete disappearance of the tumors around the left eye in just under one week.

The disease in this case had its onset at the age of 46 in the form of enlargement of lymphadenoid tissue. The first diagnosis, reticulocellular sarcoma, was based on biopsy observations. Two years later, however, the patient's physical condition was still fairly good, and, in view of developing ophthalmic signs, the diagnosis was revised to that of giant follicular lymphadenopathy. The ophthalmic signs consisted of tumorous growths in the conjunctival fornices, which growths had partly invaded the lacrimal gland. Lymphoid infiltrations, moreover, were present around the right lacrimal sac, causing phlegmonous dacryocysititis, and in the subcutis of the cheeks, lips and right temple. Similar changes were present also in the nasopharynx and, perhaps, the palate. Throughout the course of the disease the patient was troubled with congestion in the nose, and signs of sinusitis were revealed roentgenographically. Probably as a result of involvement of a lacrimal gland, bilateral keratoconjunctivitis sicca developed, being less severe in the right eye, where at an early stage the lacrimal duct was stenosed by the infiltration about the lacrimal sac. This symptom improved considerably in the left eye after its lacrimal duct had been closed by diathermy. Transient symptoms or complicating diseases occurred in the form of changes in the skin 2½ and 3½ years, respectively, after the onset of the original disorder. On one occasion the eruptions were impetiginoid, and on the other they resembled erythema multiforme exudativum. Just less than three years after beginning of the illness, typical herpes zoster developed on the left side of the thorax. From the very beginning of the disease laboratory tests disclosed the presence of pathological changes in the protein composition of the plasma and a fairly considerable eosinophilia. Roentgen therapy was prescribed, with very satisfactory results on several occasions. The size of the lymph nodes and lymphoid infiltrations decreased as early as within a few days, but after several months there was an exacerbation of symptoms. A similar good effect resulted also from the intravenous injection of 2.5 millicuries of radioactive phosphorus. Penicillin treatment (up to 1,000,000 units in 24 hours), however, had no effect on the lymph nodes. After four years of the disease, the patient is still in good condition, and his body weight is almost unchanged.

COMMENT

In some respects the symptoms in this case differ from the usual picture of giant follicular lymphadenopathy. Judging from a review of the cases previously published, it seems that the changes in the compo-

sition of the blood proteins, which were striking in this patient, are rare. Usually the sedimentation rate is normal. Heintzelmann[7] (1945), however, described a case in which it was considerably increased. He obtained values between 118 and 144 mm. in one hour. In his case, a gel formed quickly in the "formol"-gel test; the total protein content was slightly increased, chiefly owing to a rise in the globulin fraction (5.4 to 3.9 Gm. per 100 cc., as against the normal values, according to Hammarsten,[8] of 1.2 to 2.3 Gm. per 100 cc.), but also because of a relative decrease in the albumin fraction (3.6 to 3.8 Gm. per 100 cc., as compared with normal values of 4.6 to 6.7 Gm. per 100 cc.). In the present case, also, the protein composition was similarly altered, a change which probably was responsible for the positive result in several of the clinical laboratory tests, e. g., the Takata-Ara test. It may be questioned, also, whether the unusual results of the tests for syphilis had not the same cause. The patient denied having had syphilitic infection, and the reactions were always uncharacteristic. It is interesting to note here that in a case of giant follicular lymphadenopathy described by Ljungdahl-Östberg and Mårtensson,[9] that of a woman aged 45, the patient had not to her knowledge been infected with venereal disease (she was a virgin as well); nevertheless, the reaction to Meinicke's test was positive.

Hyperglobulinemia is fairly often associated with various changes in the lymphatic system and with chronic infectious diseases; consequently, its presence in giant follicular lymphadenopathy cannot be considered surprising.

The absence of anemia and the normal white blood cell count are characteristic of giant follicular lymphadenopathy. A very high degree of eosinophilia is not very common, however, even if instances have been described previously.[10] There is no likely explanation for the latter symptom. Thus, there was no helminthiasis, no asthma, no hayfever. The biopsy specimens were examined to determine whether eosinophils were present, but none were found (Prosector S. Ranström).

In the present case, not only were the pathological changes located in the regional lymph nodes and the spleen, but there seemed also to exist a pronounced tendency to infiltration of the subcutis and the submucosa of the face, oral cavity and pharynx. The prolonged disturbance of the sinuses and the roentgenographically visualized mucosal swelling

7. Heintzelmann, F.: Giant Follicle Lymphadenopathy (Follicular Reticulosis—Brill-Symmers' Disease), Acta med. Scand. **124**:359, 1946.

8. Hammarsten, G.: Klinisk kemi, in Astra: Kliniska laboratoriumsmetoder, Stockholm, 1947.

9. Ljungdahl-Östberg, K., and Mårtensson, E.: Två fall av Symmers syndrom, in M. Ljungdahls Festskrift: Om sjukdom och sjukvård, Gleerup, Lund, 1947.

10. Heintzelmann,[7] Salm, R.: Het lymphoblastoma folliculare; Dissertation, Amsterdam, 1939.

in the paranasal sinuses might have had the same cause. Such a tendency seems not to have been present to the same degree in any case yet published. In this respect, therefore, the picture exhibited some similarity to leukemia or lymphosarcoma.

In the present case the ophthalmic symptoms dominated and caused the most distress. On their account the patient was unable to work for most of the past six months. As the treatment has kept the symptoms practically in check, he now has been able to resume work. The pathological lymphoid tissues were probably in the main localized to and around the anterior orbital region. It is difficult to say where the infiltrations came from, but they were first seen in the upper fornices, and in the biopsy sample the pathological infiltrations were conjoined with the lacrimal gland, in which similar cellular elements were interspersed. The lacrimal glands had therefore probably been involved in the pathological process from the very beginning. In the course of the growth, the neighboring skin had also been infiltrated, the process finally including the walls of the lacrimal sac on the right side and resulting in phlegmonous dacryocystitis. The patient's typical symptoms of keratoconjunctivitis sicca were certainly secondary to the changes in the lacrimal glands, which had given rise to reduced lacrimation. That such symptoms may develop in pathological infiltration of the lacrimal glands, especially in sarcoidosis (Schaumann's disease), has been described earlier in the literature (von Bahr [11]). I have previously observed one such case, in which the changes were bilateral, lacrimation was practically abolished and typical changes were present in the cornea and conjunctiva. In this patient, too, the keratoconjunctivitis responded remarkably well to closure of the canaliculi.

Ophthalmic symptoms are probably not the most characteristic signs of giant follicular lymphadenopathy, but have, nevertheless, been reported in a rather large proportion of cases. Thus, it has been pointed out [6] that the tendency to lymphoid infiltration in the lacrimal glands, giving rise to exophthalmos, is characteristic of giant follicular lymphadenopathy. Among other things, this assertion is probably based on an article by Rosenthal, Harris and Kean,[12] in which are tabulated the data on four patients with giant follicular lymphadenopathy, all of them women, who had exophthalmos. In two of these patients it was the first symptom. In a review by Ross [13] of noninflammatory enlargement of the lymphadenoid tissue are described two cases of "lymphoid follicular reticulosis,"

11. von Bahr, G.: Case of Uveo-Parotitis with Perivasculitis and Other Rare Symptoms, Acta ophth. **16**:101, 1938.

12. Rosenthal, N.; Harris, W., and Kean, A.: Clinical and Radiotherapeutic Considerations of Follicular Lymphoblastoma, Am. J. Roentgenol. **29**:95, 1933.

13. Ross, J. M.: Classification of Non-Infective Enlargement of Lymph Nodes, Brit. M. J. **2**:1029, 1939.

which apparently is identical with giant follicular lymphadenopathy. It was mentioned that in one of these cases there was proptosis of the left eye, and enlarged glands were found about the left orbit. Another case with exophthalmos was reported by Baggenstoss and Heck.[14] In one of Heintzelmann's two cases, one of the first symptoms was swelling of the eyelids, owing to enlarged lacrimal glands. Lastly, Goedbloed and Wijers [15] have described the case of a man aged 69 who had tumors around the orbital opening on both sides and who earlier had had roentgen-sensitive lymphadenitis in the right groin and later also in the left groin, with secondary edema of the legs and a tendency to relapse. The orbital tumors were extirpated, but the changes returned. There developed gradually exophthalmos and inhibited mobility of one eye with diplopia. These symptoms disappeared completely after treatment with roentgen irradiation in small doses; when the changes on the contralateral side took on a similar appearance, they also were given the same treatment with the same results. Biopsy disclosed the presence of lymphoid tissue with very large and more or less rounded islets, which were very similar to enormous lymph follicles, and, in addition, a structurally discrete interfollicular tissue. Staining for reticulin revealed a more prominent alveolar architecture than sometimes may be seen in normal lymph nodes. This was plainly a case of giant follicular lymphadenopathy, and the authors were of that opinion.

Several cases of "lymphoma" in the conjunctiva have been described in which giant follicular lymphadenopathy may possibly have been present, but in which the reader cannot easily make a diagnosis on the basis of available facts. Thus, giant follicular lymphadenopathy might have been present in four cases of conjunctival lymphoma described by Ennema.[16]

Cases of lymphoid infiltration in the wall of the lacrimal sac have likewise been described. For example, as early as 1928 Weve [17] reported the case of a woman aged 59 who was operated on for tearing due to swelling of the lacrimal sac. The irregularly thickened wall of the lacrimal sac on histologic examination was seen to contain lymphoid tissue with, among other things, typical growth nuclei. Later examination revealed a swollen lymph node on the right side of the neck. The blood picture was normal. A complication in the healing of the operative wound

14. Baggenstoss, A. H., and Heck, F. J.: Follicular Lymphoblastoma (Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen), Am. J. M. Sc. **200**:17, 1940.

15. Goedbloed, J., and Wijers, H. J. G.: Lymfoblastoma Folliculare (Mitteilung eines Falles mit Augensymptomen), Acta ophth. **19**:28, 1941.

16. Ennema, M. C.: Lymphoma Conjunctivae, Acta ophth. **13**:225, 1935.

17. Weve, H. I. M.: Een lymphatische tumor van den traanzak, Nederl. tijdschr. v. geneesk. **1**:696, 1928.

cleared after a single roentgen treatment. It is not unlikely that this case was one of giant follicular lymphadenopathy. A similar conclusion applies to the case of a woman described by Sédan, Astier and Caudière[18] (1931). This woman had phlegmonous dacryocystitis, and the sac was incised. A nonsensitive tumor was found after 30 days in the region of the lacrimal sac; the tumor had invaded the orbit. At that time the patient had double vision. On removal, the lacrimal sac proved to be heavily lobulated, so that it resembled pancreatic tissue or salivary gland. The diagnosis of "lymphoblastoma" was made on histologic examination. Roentgen treatment of the orbital tumors was highly satisfactory. In due course the lymph nodes in the neck began to swell, as did those in the axillas and the mediastinum. The patient died in dyspnea and cachexia seven months later.

Tumors in the lacrimal sac are rare. Cases of carcinoma and sarcoma have been described. In giant follicular lymphadenopathy the changes may evidently be confined to the wall of the lacrimal sac, and it is not improbable that many cases of so-called lymphoma in and around the lacrimal sac and in the conjunctiva in actual fact may prove to be cases of giant follicular lymphadenopathy.

SUMMARY

A case of giant follicular lymphadenopathy with prominent ophthalmic symptoms is described. After the patient had had generalized lymphadenoid enlargement for two years, lymphoid infiltrations entered the conjunctival fornices of the eyes. It could be demonstrated that the lacrimal tissue was infiltrated; and when phlegmonous dacryocystitis later developed on the right side, this infiltration proved to be due to similar changes in the wall of the lacrimal sac. Similar infiltrations appeared in the buccae, and possibly in the palate and nasopharynx. Probably as a secondary phenomenon to the involvement of the lacrimal gland, keratoconjunctivitis sicca developed and was successfully treated by means of canalicular diathermy.

Cases of the same disorder with similar involvement of the lacrimal gland have been described earlier, but the phlegmonous involvement of the lacrimal sac in this case seems to be a symptom so far unrecorded in this disease. However, it is not improbable that in earlier cases of so-called lymphoid infiltration in the wall of the lacrimal sac, the diagnosis may have been that of giant follicular lymphadenopathy.

18. Sédan, J.; Astier, A., and Caudière, M.: Lymphoblastome du sac lacrymal généralisé aprés étape orbitaire, à la totalité de l'appareil lymphatique, Bull. et mém. Soc. franç. d'opht. **44**:249, 1931.

THE PTERYGIUM

Brief Review and Evaluation of Certain Methods of Treatment

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THE INCIDENCE of pterygium among military personnel in semitropical Hawaii is higher than in most sections of the United States; however, its frequency does not approach that of the more tropical countries. A uniform satisfactory treatment of this ancient problem is far from achievement. One who sees many pterygiums cannot help but be impressed by the large number which have previously been treated surgically. In the published series recurrence rates vary. One may justifiably suspect that in a series in which no failures are reported the patients have not been carefully followed.

During the past 18 months, my colleagues and I have treated 300 patients with pterygium at this hospital. In about one third the lesion was recurrent, and previous operation had been done elsewhere. The obvious failure of the usual method of treatment prompted us to employ various technics, in an effort to determine the most satisfactory treatment.

ETIOLOGY AND PATHOLOGY

The etiology and pathology will not be discussed. We agree with those who feel that the pterygium is a result of chronic conjunctival inflammation from various causes.[1] We subscribe to the proposition that the degenerative changes in the subconjunctival tissues are entirely secondary to inflammation, and are not due to primary degeneration. The process begins as "chronic irritative exposure conjunctivitis."[1] When the cornea becomes involved, the resulting chronic keratoconjunctivitis leads to encroachment of conjunctival tissue on the cornea. Changes in the cornea may be due to impaired nutrition, the result of involvement of the limbal circulation by the subconjunctival lesion.

1. Kamel, S.: Pterygium: Its Nature and a New Line of Treatment, Brit. J. Ophth. **30**:549 (Sept.) 1946.

TREATMENT

The numerous methods advocated for treatment of pterygium attest to the failure of any one procedure to effect a cure universally. The various modes of treatment in modern use may be summarized under the following heads: (1) transplantation, (2) excision, (3) excision and movable flap repair, (4) "bare sclera" methods; (5) grafting and (6) irradiation. Less popular methods, including cauterization by chemicals [1] or direct heat [2] and electrosurgery,[3] will not be discussed. Modifications of these general operative measures are too numerous to permit mention of all of them. Each has been endorsed by its originator and no doubt yields good results when properly applied.

1. *Transplantation.*—The most generally used surgical treatment of pterygium in this country, and probably throughout the world, is the McReynolds transplant.[4] The technic needs little explanation (figure, *A* and *B*). Its almost universal acceptance has been based on its claims of simplicity and general efficiency. Any one who has employed this technic over a period of years has soon begun to doubt its ultimate curative value. Recent reports indicate that it is not functioning well in the hands of many ophthalmologists. D'Ombrain [5] and Kamel [1] listed recurrence rates of 30 to 50 per cent after McReynolds' transplantation. The latter stated that it is successful only with atrophic inactive pterygiums, in which inflammation has completely subsided. In cases of this type, he stated, simple excision is more satisfactory and less mutilating. Rosen [6] expressed the opinion that recurrence following McReynolds operation is the rule even in the hands of the experienced ophthalmic surgeon. This method was followed in 75 cases in our series. The technic was modified slightly by burying the head of the pterygium superiorly in the majority of cases and by scarifying it to insure coaptation with the subconjunctiva and prevent slipping. In 12 of these cases the condition has recurred. There was no evidence of the head's slipping in any case. The new growth invaded the cornea from the side of the buried transplant.

The McReynolds transplantation was followed by cautery of the limbal area in eight cases of hyperemic, "malignant" pterygium, in four of which there was recurrence. This obliterated all blood vessels

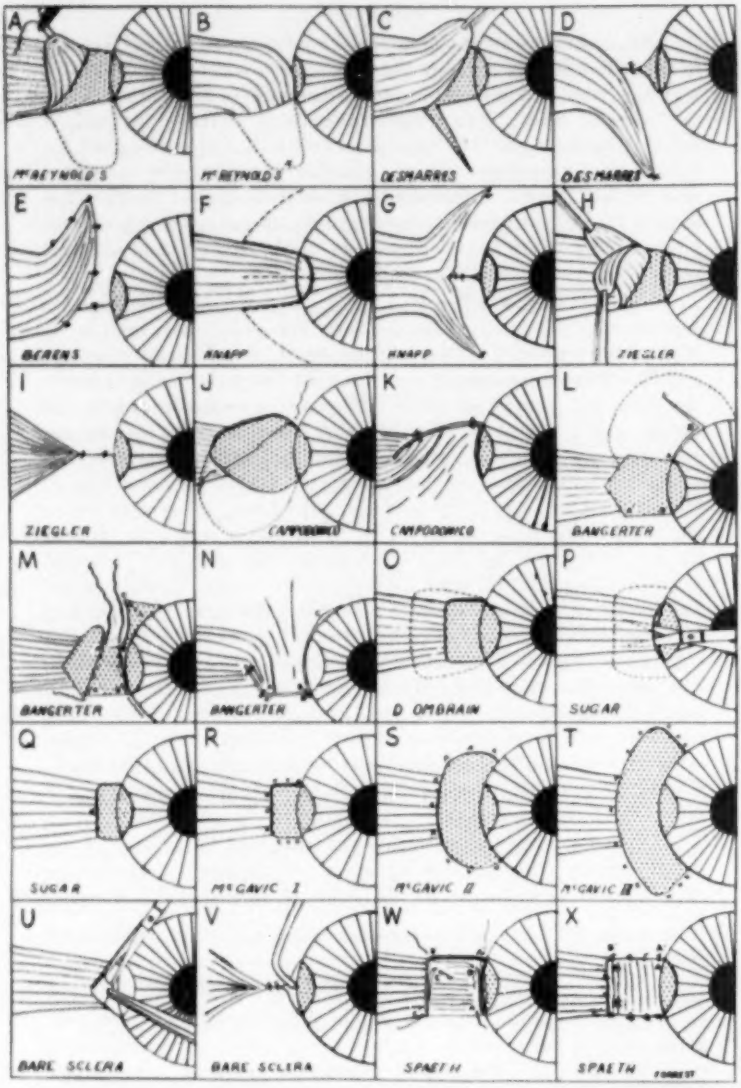
2. Zubak, M. F. C.: Electrocoagulation of Pterygia, Arch. Ophth. **5**:732 (May) 1931.

3. Kirby, D. B.: Electro-Surgical Excision of Pterygium; New Method, Am. J. Ophth. **26**:301 (March) 1943.

4. McReynolds, J. O.: The Nature and Treatment of Pterygia, J. A. M. A. **39**:296 (Aug. 9) 1902.

5. D'Ombrain, A.: The Surgical Treatment of Pterygium, Brit. J. Ophth. **32**:65 (Feb.) 1948.

6. Rosen, E.: Pterygium, Brit. J. Ophth. **32**:300 (May) 1948.



Diagrammatic presentation of various technics advocated for treatment of pterygium.

and left an area of bare sclera several millimeters wide. Phenol and alcohol were used in four cases, and the hot muscle hook was employed in the other four. There has been one recurrence in this group.

Desmarres [7] (figure, *C* and *D*) is credited with the origin of the first operation to transplant the head of a pterygium by carrying it down into a conjunctival slit below, suturing it as a pedicle flap. Miller [8] modified this operation, making paracorneal incisions to close the conjunctival defect and to overlap the denuded corneal margin. Miller secured the growth in its new position by supporting sutures on each side. Berens [9] further altered this technic by transplanting the pterygium sharply upward (figure, *E*). McReynolds' modification of Desmarres' technic claims the advantage of eliminating the area of exposed sclera at the limbus.

Ziegler [10] reported greater success with the McReynolds operation by excising the subconjunctival tissue before transplanting the head. Goldenburg [11] removed the underlying pterygeal tissue with a curet. He then performed the McReynolds transplantation, carrying the head suture through the lower lid and tying it over rubber tubing on the skin surface.

Neher [12] modified McReynolds' procedure by transplanting the pterygium beneath the upper bulbar conjunctiva. Goldsmith [13] sutured the transplanted head to the episclera under direct observation.

Rosen [6] stated that he favors folding the pterygium back on itself after undermining the entire growth. The suture is brought out through the caruncle and tied over a rubber button. The conjunctival edges are then sutured together from the buckled end of the pterygium to the limbus. This inverted transplant was employed by us in treatment of four hyperemic growths, three of which were previously recurrent. The pathological tissue was diverted 180 degrees. The resulting bulge gave a poor cosmetic result. Although there were no recurrences, the procedure was discarded because of slow healing, accompanied with much discomfort to the patient from the rubber peg at the caruncle.

7. Desmarres, L. A., cited by Weiner, H.: Am. J. Ophth. **11**:876 (Nov.) 1928.

8. Miller, H.: Modification of Desmarres' Operation for Transplantation of Pterygium, Am. J. Ophth. **20**:165 (Feb.) 1937.

9. Berens, C., in discussion on Neher, E. M.: New Method for Transplanting Pterygium, Arch. Ophth. **21**:30 (Jan.) 1939.

10. Ziegler, S. L.: The Subconjunctival Excision of Pterygium, International Congress of Ophthalmology, Philadelphia, 1922, vol. 1, p. 205.

11. Goldenburg, M.: Pterygium Surgery, Proc. Chicago Ophth. Soc., Nov. 21, 1921; abstracted, Am. J. Ophth. **5**:256 (April) 1922.

12. Neher, E. M.: A New Method of Transplanting Pterygium, Arch. Ophth. **21**:30 (Jan.) 1939.

13. Goldsmith, J.: A New Modification of the McReynolds Transplantation for Pterygium, Arch. Ophth. **37**:194 (Feb.) 1947.

Knapp's [14] technic has been advised for a pterygium with a very broad head. The entire pterygium (figure, *F* and *G*) is split by a horizontal incision. This is followed by two incisions, outlining the upper and lower margins of the growth to about half its length. Each incision is then carried toward the limbus, one arching above and the other below. Each half of the pterygium, now a movable flap, is then sutured into its corresponding conjunctival slit, above and below. We performed this operation in nine cases, in two (22 per cent) of which the lesion recurred in three months. With this method the conjunctiva is spared and the defect is minimized. The operation takes more time to perform, and the wound is slower in healing than in most other methods.

2. *Excision* (resection).—This was the method of treatment in use in the year 1 A. D. The technic of Arlt,[15] introduced over a century ago, is well known and still has advocates. The pterygium is totally excised to a point near the caruncle. The rhomboid defect remaining is covered by uniting the upper and lower margins by several interrupted sutures. Fuchs stated that relapses were not infrequent after Arlt's technic. Berens [16] added that none but very small pterygiums can be removed by excision without a recurrence being expected. We have used this method, with good results, in five cases. It is a simple procedure, rapidly carried out, and the pathological tissue is totally removed. However, it may be used only for small, early growths. We feel that there are better methods for treating pterygiums of this type.

Ziegler [10] (figure, *H* and *I*) performed partial excision by dissecting the subconjunctival tissue free and totally removing it. The flap of conjunctival epithelium is allowed to remain in place after the head is removed. The defect is closed by suturing the undermined conjunctival edges from above and below. Paracorneal incisions are used if necessary to relieve tension, and several "pie cut" incisions may be made in the conjunctiva if it overlaps the cornea. The juxtacorneal suture is anchored in the sclera, and the conjunctiva is closely alined with the cornea. Wadsworth [17] modified this method by using a large lamellar keratoplasty trephine to make a circle in the cornea of sufficient area and depth to include the entire head of the pterygium. The section of cornea outlined is dissected back beyond the limbus and excised, along with adjacent involved conjunctiva. Closure of the defect is similar to that in Ziegler's method.

14. Knapp, H.: New Plastic Conjunctival Operation, Arch. f. Ophth. **14**:267, 1868.

15. Arlt, F. R., cited in Fuchs, E.: Textbook of Ophthalmology, Am. ed. 2, New York, D. Appleton & Co., 1903, p. 115.

16. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, vol. 20, p. 1078.

17. Wadsworth, J. A. C.: Personal communication to the author, 1949.

3. *Excision and Movable Flap Repair.*—Campodónico [18] (figure, *J* and *K*) excised the pterygium, leaving an oval bare area. This is closed by bringing up a flap of conjunctiva from the lower outer angle of the defect to the limbus above, where it is joined to the conjunctiva with a suture anchored in the episclera. Spaeth states that this method is uniformly satisfactory for small pterygiums. He feels that a recurrence is almost impossible because the direction of the conjunctival vessels is changed and the wound is closed at the limbus with healthy conjunctiva. We have found this to be a very satisfactory treatment for early pterygium. It can be performed simply and rapidly. It heals well, with a good cosmetic result, making it especially preferred for women. There have been three recurrences in 50 cases. The following modification is useful with larger growths. After the pterygium is excised, the limbal defect is carried a millimeter or so above, into healthy conjunctiva. The lower inner flap is brought up and anchored to conjunctiva at the limbus, leaving several millimeters of bare sclera adjacent to the limbus. There have been no recurrences in 26 cases.

Bangerter [19] (figure, *L*, *M* and *N*) excised the pterygium in a manner which leaves a rhomboidal defect. A paracorneal incision is then made above from *A* to *B*, its length coinciding with the lower border of the conjunctival defect. The bulbar conjunctiva is undermined above to the midline. A second incision is made from *B* to *C*, slightly divergent but almost parallel to the upper border of the defect. The length of this incision coincides with the conjunctival defect at the limbus, where the head of the growth was excised (*A-B'*). This free tissue is then used as a sliding flap to cover the defect. A silk suture from point *A* is anchored in the episclera at *A'*. Point *B* is similarly brought down to *B'* and anchored next to the limbus in the episclera. Several additional interrupted sutures may be used to close the remaining margins. Any overlapping portion on the cornea should be excised. We have found a modification of Bangerter's technic more satisfactory. The growth is excised, leaving a more quadrilateral defect, extending 1 to 2 mm. below the limbus into healthy conjunctiva. Point *B* is sutured to the episclera below the lower margin of the original pterygium. A millimeter or so of bare sclera is left at the limbus. This procedure is extremely valuable in treating a large, active pterygium and most recurrent lesions. It may be impossible to perform in patients with abundant scar tissue caused by several recurrences. Bangerter's procedure has been followed in 40 of our cases, with one failure. The modification described was applied in 20 of these, and there has been no recurrence in this group.

18. Campodónico, E.: A New Procedure in the Excision Method of Pterygium Operation, International Congress of Ophthalmology, Washington, D. C. **1**:201 (April) 1922.

19. Bangerter, A.: Pterygium Operation and Covering of Conjunctival Defects. Ophthalmologica **106**:316 (Dec.) 1943.

4. *"Bare Sclera" Methods.*—In the past, many [20] authors have claimed that a successful operation for pterygium demands close approximation of "healthy" conjunctiva at the denuded limbus. Spaeth stated the belief that it is not surgically sound to permit this denuded area at the limbus to heal by granulation. Several recent publications,[21] however, have advocated a defect of denuded sclera, of varying size, at the limbus. All such procedures should be termed "bare sclera" technics.

D'Ombrain [21a] (figure, *O*) excises the submucosal tissue back to the caruncle, leaving a quadrilateral bare strip about 4 mm. wide at the limbus. No sutures are used. He has practiced this method for eight years, with no recurrences. Sugar's [21b] procedure (figure, *P* and *Q*) is similar except that subconjunctival tissue, including Tenon's capsule, is excised through an incision in the head of the pterygium at the corneal limbus. The remainder of the head is then shaved off the cornea. The cut edge of conjunctiva is sutured to the sclera 3.5 mm. from the limbus; a bare area of sclera 3 mm. in width is left adjoining the cornea. No recurrence has been noted in his 50 cases.

McGavic [22] advised a "bare sclera" technic for recurrent pterygium in which the subconjunctival scar tissue is excised and the conjunctiva is "recessed" from the limbus. The conjunctiva alone is secured to the episclera by interrupted sutures placed about 2 mm. apart and at least 5 mm. from the limbus. The bare area is allowed to epithelize. He performs three grades of "baring": one in which the conjunctiva is not recessed beyond the vertical limits of the pterygium (figure, *R*); another, in which limbal incisions are made 3 mm. above and below the attachment and the conjunctiva is sutured to the sclera 5 mm. from the entire limbal area (figure, *S*), and the third (figure, *T*), in which the recession is done 5 mm. above and below the corneal attachment of the growth, as well as 5 mm. toward the canthus. The sutures are removed on the tenth day.

We independently have used a procedure similar to the McGavic grade 2 technic in several cases of severe multiple recurrence complicated by diplopia, resulting from the limitation of motion due to contraction of scar tissue. In all these cases, after one year of observation, there is complete quiescence, with a good functional and cosmetic result. Our routine bare sclera technic, as described below, is somewhat more conservative than the grade 1 procedure of McGavic. Since publication of

20. (*a*) Ziegler.[10] (*b*) Spaeth, E. B.: Principles and Practice of Ophthalmic Surgery, ed. 4, Philadelphia, Lea & Febiger, 1948, p. 593.

21. (*a*) D'Ombrain, A.: Surgical Treatment of Pterygium, Brit. J. Ophth. **32**:65 (Feb.) 1948. (*b*) Sugar, H. S.: Surgical Treatment for Pterygium, Am. J. Ophth. **32**:912 (July) 1949.

22. McGavic, J. S.: Surgical Treatment of Recurrent Pterygium, Arch. Ophth. **42**:726 (Dec.) 1949.

his technic, we have employed the grade 3 method, described above, in 10 cases of severe recurrence. In two cases the lesion has recurred again. We feel that this procedure should be reserved for intractable recurrences. There is much postoperative discomfort. Healing is slow, and the eye remains inflamed for a month or longer.

The "bare sclera" method which we have used for the past 18 months may be termed a modification of d'Ombrain's [23a] operation. Briefly, the technic is as follows (figure, *U* and *V*):

The head is dissected from the cornea with a Bard-Parker knife (no. 15 blade). The dissection is begun from clear cornea in the manner of a superficial keratectomy. The entire pterygium is undermined along the sclera. The epithelial surface of the conjunctiva is then separated from the subconjunctival tissues, and the subconjunctival tissue is totally excised. The apex of the head is then removed by two converging snips of the scissors, leaving a diamond-shaped defect of cornea and conjunctiva. The conjunctiva is undermined above and below, and two interrupted 0000 black silk sutures are used to approximate the separated edges. A bare area 2 mm. wide is left at the limbus. This area is cauterized by a hot muscle hook to obliterate any episcleral vessels. The procedure is surgically sound, for the following reasons: First, the pathological tissue comprising the pterygium is totally removed, and is not buried or diverted; second, there is minimum loss of conjunctiva; third, the scleral vessels near the limbus are eliminated by cautery; fourth, the area of bare sclera allows the conjunctiva and cornea to heal separately (the conjunctival epithelium rapidly grows over the scleral defect, but not until the cornea has healed first); fifth, the cauterized bare sclera acts as a barrier, much as does a free graft of skin or mucous membrane when placed at the limbus in operations for recurrent pterygium, and, sixth, the cosmetic and functional results are excellent. There have been six recurrences in 53 cases of pterygium treated by this method. It may be used for either primary or recurrent pterygium; however, all recurrences in this series were in cases in which a previous operation had been performed by some other method.

5. *Grafting.*—Most operative methods employing a graft are advocated for the recurrent pterygium. Some [23] have been used to cover large conjunctival defects after primary removal of nonrecurrent pterygiums.

Conjunctival Grafts: Elschnig [24] used a conjunctival flap to close the wound defect after removing a recurrent pterygium. This flap, with upper and lower peduncles, was dissected from the limbus of the healthy side

23. Wiener, M.: Treatment of Recurrent Pterygium, Am. J. Ophth. **11**:876 (Nov.) 1928; citing Klein, S.: Zur Operation des Pterygium und zur Transplantation vom Schleimhaut, Allg. Wien. med. Ztg. **21**:19; 29, 1876.

24. Elschnig, H. H.: A New Operation for Relapsing Pterygium, Klin. Monatsbl. f. Augenh. **76**:714, 1926.

of the cornea and then moved over and sutured between the cornea and the margin of the pterygium. Gómez-Márquez [25] covered the defect with a conjunctival flap taken from the upper bulbar conjunctiva of the other eye. Spaeth [26] devised a "rotated island graft," which he stated is particularly applicable in exceptionally severe cases and in recurrent pterygium. This ingenious procedure is much simpler than it at first appears. The resulting rotated rectangular area of conjunctiva contains the pterygium. Thus, the direction is changed 90 degrees, either up or down (figure, *W* and *X*). After the head of the pterygium is torn from the cornea by a suture (we prefer sharp dissection), three sides of the rectangle are outlined by incising the conjunctiva with sharp scissors. A suture is passed through each corner of this island and then anchored in the episclera and conjunctiva of the next corner of the defect in the direction the flap is to be rotated. The "island" is then completed by incising its lower margins, and the sutures are secured. The block is thus caused to rotate to the anchored corners. Additional, smaller sutures are then placed between the four corner-anchoring sutures. Care is taken to prevent the graft from overlapping denuded cornea. Blatt [27] modified this operation by rotating the conjunctival island flap 180 degrees, instead of 90 degrees, thus completely reversing the direction of the pterygium.

This procedure is useful for extremely large, hyperemic pterygiums or for multiple recurrences. It avoids the loss of conjunctiva; however, the wound is very slow healing, and the eye presents a poor cosmetic appearance for a considerable time. It was used in 10 cases of severe, recurrent pterygium, in one of which the lesion recurred within two months.

Mucous Membrane Grafts: Klein, in 1876, cited by Wiener,[28] recommended mucous membrane grafts to replace the conjunctiva in large defects for nonrecurrent pterygiums. The use of these grafts is at present limited almost entirely to treatment of recurrent pterygiums and of those with extensive loss of conjunctiva.

Duverger [28] and Mata [29] favored the use of a mucous graft from the inner side of the lower lip, which is sewed between the cornea and the cut conjunctival edges. Spaeth [30] recommended that the graft be taken from

25. Gómez-Márquez, J.: New Operative Procedure for Pterygium, Arch. de oftal. hispano-am. **31**:87 (Feb.) 1931.

26. Spaeth, E. B.: Rotated Island Graft Operation for Pterygium, Am. J. Ophth. **9**:649 (Sept.) 1926.

27. Blatt, N.: Replantation of Pterygium as a Method of Operation for Pterygium, Ztschr. f. Augenh. **76**:161 (Jan.) 1932.

28. Duverger, C.: Extirpation of Pterygium and Transplantation of Buccal Mucous Membrane, Arch. d'opht. **43**:705 (Dec.) 1926.

29. Mata, P.: Surgical Treatment of Pterygium with Mucous Autoplasty, Arch. de oftal. hispano-am. **31**:177 (March) 1931.

30. Spaeth,[26b] p. 313.

the buccal surface. One should allow for about 10 per cent shrinkage of this tissue.

Panzardi [31] used amniotic membrane as a transplant to the conjunctival defect in 11 cases of pterygium.

Free grafts were used in 10 cases of multiple recurrence. In three of these there was diplopia, due to restriction of lateral motion of the globe. In three cases conjunctiva from the upper and lower cul-de-sacs was placed in a strip covering only the limbal defect. In another three cases, in which recurrence had acted as symblepharon, mucous membrane from the inner lip was used to cover large semilunar defects adjoining the limbus. The available conjunctiva was needed to reform the cul-de-sacs. In four cases of repeatedly recurrent growths, a small strip of buccal mucous membrane was placed at the denuded limbus. There have been no recurrences in this group. These grafts are slow healing and give poor cosmetic results. They should be used only for very severe recurrence when other methods have failed.

Epithelial Grafts: Thiersch grafts, for recurrent pterygium, were advocated by Hotz [32] in 1892. Gifford [33] used the same type of graft for recurrent pterygium, leaving bare the cornea and several millimeters of sclera at the limbus. Wiener [23] stated the belief that the epithelial graft is the only method which has proved universally satisfactory in cases of recurrent pterygium. The apex of the growth is removed from the cornea and excised flush with the limbal attachment. The body of the pterygium is then undermined. A small, very thin epithelial graft is shaved from the flexor surface of the arm or forearm. This is trimmed into a strip several millimeters wide and 6 to 8 mm. long and is then teased under the cut conjunctival edge, with its long margin slightly lateral to the limbus and not overlapping the cornea. No sutures are used. If desirable, for cosmetic reasons, the graft may be peeled off after six months. According to Wiener, there is little danger of recurrence of the pterygium.

Corneal Grafts: The use of keratoplasty is not new in the treatment of pterygium. It was first recommended by Magitot [34] in 1916. The pterygium is removed from the cornea, and a conjunctival flap is prepared at the limbus to cover this section. A semicircular incision is made on the upper part of the cornea of the same eye close to the limbus, with its base up. A flap of the superficial layers of the cornea is separated and placed

31. Panzardi, D.: Use of Fetal Membranes as Material for Plastic Restoration of Conjunctiva, with Special Regard to Their Use in Pterygium, Boll. d'ocul. **26**:332 (May) 1947.

32. Hotz, F. C.: A Few Experiments with Thiersch Grafts in the Operation for Pterygium, J. A. M. A. **19**:297 (Sept. 10) 1892.

33. Gifford, H.: Treatment of Recurrent Pterygium, Ophth. Rec. **18**:1 (Jan.) 1909.

34. Magitot, A.: A Critical Study of Certain Biological Properties of the Corneal Tissue and of Human Keratoplasty, Ann. d'ocul. **152**:417 (Oct.) 1916.

over the area of the cornea from which the pterygium was removed. The corneal graft is held under the previously prepared conjunctival flap. A similar operation is done by Filatov, who takes the corneal graft from other eyes, including those of a fresh corpse.

Reis [35] performs a McReynolds transplantation of the head after deep dissection of the growth from the cornea with a Graefe knife. He prepares a conjunctival flap under this at the denuded limbus. A superficial layer of cornea is removed from a freshly enucleated eye after delimiting its margins by two shallow incisions with a Graefe knife. The width of the graft varies from 3 to 5 mm., depending on the extent of denuded cornea to be covered. The graft is transferred to the corneal defect and is slid partly under the conjunctival flap. Reis stated that this procedure gives better optical and cosmetic results and seems to prevent recurrences.

Kilgore, according to Castroviejo,[36] stated that an extensive pterygium is an indication for superficial keratectomy with or without grafting. This is especially true in cases of recurrent pterygium.

Corneal grafting will no doubt continue to be employed for occasional severe cases of recurrent pterygium; however, it does not appear to be destined to take a prominent place in the treatment of pterygium.

6. *Radiation.*—Roentgen Radiation: Many authors have noted the efficacy of roentgen therapy in treatment of pterygium. Torres Estrada [37] recommended its postoperative use in cases in which recurrence was considered likely. Wiener [38] stated that recurrence can usually be prevented by several mild erythema doses of roentgen radiation given at intervals of two to three days after operation. Hilgartner, Wilson and Wilson [39] reviewed their results of postoperative irradiation of 10 patients. No evidence of recurrence was noted in any patient, and some were followed for two years. The authors recommended this treatment to prevent recurrence after surgical removal of large vascular pterygiums. They stated that roentgen irradiation is contraindicated for the small, avascular pterygiums. Its value is thought to be due to the inhibiting action of roentgen rays on immature epithelial cells, connective tissue and blood vessels.

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35. Reis, J. L.: A Corneal Graft Operation for Recurrent Pterygium, Brit. J. Ophth. **29**:637 (Dec.) 1945.

36. Castroviejo, R., in Spaeth,[20b] p. 647.

37. Torres Estrada, A.: Treatment of Pterygium, J. Internat. Coll. Surgeons **3**:219 (June) 1940.

38. Wiener, M.: Surgery of the Eye, ed. 2, New York, Grune & Stratton, Inc., 1949, p. 195.

39. Hilgartner, H. L.; Wilson, R. T., and Wilson, J. D.: Surgical Treatment of Pterygia Followed by X-Ray Therapy to Prevent Recurrence, Am. J. Ophth. **31**:667 (June) 1948.

We have employed roentgen therapy after operation in 25 cases of the progressive, vascular, "malignant" type in which recurrence appeared likely. In 11 there had been no previous operation, and in 14 the lesion was recurrent. In five of the latter there had been more than one previous operation. The procedure used, which is similar to that of Hilgartner's, is as follows:[40]

Treatment is begun on the fifth to the seventh postoperative day, when the sutures are removed, and is repeated every four to five days. An average of five treatments is given in about a three week period. The dose of each treatment is approximately 200 r, and a total of about 1,000 r is administered.

There have been eight recurrences following roentgen irradiation among these 25 patients, who have been observed for 12 to 18 months. In four of the eight cases there had been a previous recurrence. One pterygium reappeared before the fifth treatment was given, and its growth seemed to be "stimulated," rather than inhibited, by roentgen radiation. This recurrence rate is approximately 33.3 per cent. With the probability of more recurrences in the future, the claims made by others for the efficacy of this treatment in smaller series of cases are discouraging.

Beta Radiation: Beta radiation given with a radon applicator has recently been added to the list of therapeutic measures for pterygium. Iliff [41] employed contact irradiation in 18 cases. He stated that in only one was the response slow and operation required. He expressed the opinion that the method is especially valuable in cases in which there is recurrence after operation. Ruedemann [42] stated that he uses beta radiation by direct application to enlarged pinguecula and early pterygium, with good results. He treats large pterygiums with spray radiation over the corneal portion and with direct application along the limbal portion. Recurrent pterygium with interstitial vascularization requires contact irradiation over most of its extent, in order to eliminate deep vascularization. Hughes and Iliff [43] stated that beta irradiation is particularly useful in cases of "malignant" pterygiums recurring after surgical removal and those associated with considerable vascularization. Spaeth [44] stated that there is no doubt that the use of beta irradiation is of great value in curing the early, smaller pterygiums. Wiener [45] stated

40. Roentgen treatments were administered by Col. Paul Paden, Department of Roentgenology, Tripler Army Hospital. Details of the technic are omitted.

41. Iliff, C. E.: Beta Irradiation in Ophthalmology, Arch. Ophth. **38**:415 (Oct.) 1947.

42. Ruedemann, A. D.: Beta Radiation Therapy, Arch. Ophth. **41**:1 (Jan.) 1949.

43. Hughes, W. F., and Iliff, C. E.: Beta Irradiation of the Eye, Am. J. Ophth. **32**:351 (March) 1949.

44. Spaeth,[20b] p. 591.

45. Wiener,[25] p. 199.

that he uses beta rays the day after operation in all cases of pterygium. He also recommended it as an added precaution against further recurrence in cases in which an epithelial graft has been placed. The Sr^{90} beta ray applicator [46] has several advantages and has been found to be highly successful in treating all types of pterygium.

This method of treatment has not been available for use in our series. Three patients with recurrence on whom we operated had previously been treated elsewhere with postoperative beta irradiation.

INDICATIONS FOR OPERATION

Many textbooks advise that no treatment be given for pterygium until it encroaches on the pupillary area of the cornea. In the opinion of some authors, the "stationary" type should be left alone entirely. Although it is well known that the growth may remain stationary for years, and some think this quiescence may be permanent, we agree with those who feel that every pterygium is at least potentially progressive. A stationary lesion may, for no apparent reason, suddenly become active and grow rapidly. Adler [47] advised operation when it is determined that a pterygium is progressive and is invading the cornea. Ziegler [19] stated that the pterygium should be removed (*a*) when it is progressive, (*b*) when it interferes with vision, (*c*) when it limits ocular motility, (*d*) when a capital operation on the globe is planned or (*e*) when it is cosmetically disfiguring.

The term pterygium implies corneal encroachment, and it is our opinion that every pterygium should be removed surgically, regardless of its stage of growth. It is an irreversible pathological condition. The earlier it is removed, the better will be the result cosmetically and functionally.

GENERAL PRINCIPLES OF TREATMENT

It is obvious from this review of surgical procedures that no one operation may be considered the "best" to be employed in the removal of every pterygium. Most young ophthalmologists are familiar with only one method of surgically treating a pterygium—the well known McReynolds transplantation. Its indiscriminate use is probably one reason that this operation has recently fallen into disrepute.

The technics which include the total removal of the primary pathological tissue involved in pterygium, namely, the subconjunctival tissue with Tenon's capsule, appear to be surgically the soundest. Sparing of the uninvolved epithelial covering of the conjunctiva when possible also

46. Friedell, H. L.; Thomas, C. I., and Krohmer, J. S.: Beta-Ray Application to the Eye, Am. J. Ophth. **33**:525 (April) 1950.

47. Adler, F. H., in Gifford, S. R.: Textbook of Ophthalmology, edited by Francis H. Adler, ed. 4, Philadelphia, W. B. Saunders Company, 1947, p. 217.

seems more sensible than radical excision, requiring complicated flaps and transplants to cover the defect. To change the direction of growth of the pterygium by any one of the numerous buried transplantation methods violates surgical principles, in that epithelium is covered by subepithelial tissue and the inflamed pathological tissues are merely diverted, in an attempt to prevent further growth.

We agree with those who advocate leaving an area of bare sclera at the limbus as a barrier against recurrence. It appears that this allows the corneal defect to heal before any conjunctival tissue can invade the area. It also seems surgically sounder to dissect carefully the pathological tissue from the cornea, rather than to practice divulsion by tearing it off with a muscle hook, suture or other forcible means. D'Ombrain [48] categorically stated that sharp dissection is the one essential for success in any operation for pterygium. He removes the head of the growth with a sharp keratome as carefully as though he were doing a cataract section.

A careful postoperative follow-up is most important in any method of treatment. The use of a vasoconstrictor ophthalmic solution for several months is advised. If at all possible, the patient should avoid the conditions which previously served as exciting causes. Dark glasses will act as a mechanical protection against wind, sand, dust and sun in certain climates.

SUMMARY AND COMMENT

The ancient problem of satisfactory treatment for the pterygium is far from solved. The cause of the condition is believed to be exposure to numerous external irritants and to other extrinsic and intrinsic factors as yet unknown. The pathology is based primarily on a chronic inflammatory reaction, associated with or followed by degenerative changes in the bulbar subconjunctival tissue. Corneal involvement may be concurrent, or it may be secondary to nutritional changes at the limbus caused by the subconjunctival lesion.

Three hundred patients with pterygium have been operated on at this hospital in the past year and a half. Of these, 85 had been operated on previously, with a total of 133 operations. To date, there have been 28 recurrences, a rate of 9 per cent. The highest rate of recurrence for a substantial number of cases followed the McReynolds transplantation method (16 per cent). In 20 of the 28 cases of recurrence, there had been a previous recurrence, and in 8 postoperative roentgen therapy had been employed (table).

To our knowledge, there is presently available no universally satisfactory method of treatment for the pterygium. The ophthalmologist should have at his command an armamentarium for the surgical treatment of this condition, just as he has for other problems of ophthalmic

48. D'Ombrain, A.: Personal communication to the author, 1949.

Data on 300 Cases of Pterygium Treated Surgically *

Operative Technic	No. of Cases	Previously Recurrent	Follow-Up Recurrences	Recurrences, %	Post-operative Roentgen Radiation Dose, r	Advantages	Disadvantages
McReynolds transplantation	75	23 (30)	12	16	22	Simple; rapid recovery; diverts blood vessels	Tendency to recurrence new tissue grows into limbus, even though head remains fixed in new position; pathological tissue not removed
McReynolds transplantation with cautery	6	5	1	13	0	Same as above; obliterates vessels at limbus in "malignant" type	Same as above
Rosen inverted transplant	4	2 (3)	0	0	0	Diverts pathological tissue 180°	Result cosmetically poor—bulge created; discomfort during healing; pathological tissue not removed
Knapp-Terrien	9	1	2	22	0	Good for broad head; spares conjunctiva	Takes longer to perform; slow healing; pathological tissue not removed
Excision (Arlt)	3	0	0	0	0	Simple; rapid recovery; removes pathologic tissue	Applicable to small early growths only; tendency to recurrence; scar in palpebral fissure
Campodónico †	78	4	3	4	0	Simple; rapid recovery; scar out of midline; removes pathological tissue; diverts remaining blood vessels	Good for early non-hyperemic growths only
[Campodónico with bare sclera	38	2	0	0	0]		
Hangerter †	60	15 (25)	1	3	0	Diverts blood vessels; removes pathological tissue	More difficult to perform; slow healing
[Hangerter with bare sclera	20	10	0	0	0]		
Mellavie	10	10 (14)	2	20	0	Removes pathological tissue	More time consuming to perform; slow healing; results may be cosmetically poor
Bare sclera	32	3	6	11	2	Simple; surgically sound; removes pathological tissue; functionally and cosmetically good for primary cases	Slower healing; scar in palpebral fissure
Spaeth's rotating flap	10	8 (13)	1	10	1	Diverts pathological tissue 90°; spares conjunctiva	More difficult to perform; slow healing; result cosmetically poor for some time; pathological tissue not removed
Free grafts	10	10 (30)	0	0	0	Prevents recurrence by acting as a "barrier"; removes pathological tissue	Difficult to perform; slow healing; results cosmetically poor; removal of graft later may be necessary
Total	300	85 (133)	28	9	25	.....	.....
Postoperative roentgen irradiation	25	14 (22)	8	32	..	.....	.....

* The number in parentheses is the total number of previous operations in that category.
† The procedure and numbers in brackets are included in the procedure immediately above.

surgery. Much of the success of an operation for pterygium depends, of course, on the surgical skill of the operator. Goar [49] stated that the impression that any one can remove a pterygium is not justified by the results. A good operative method poorly executed may end in recurrence. The necessity of using the pterygium in training interns and residents in surgical technic may account for a higher percentage of failures in some centers.

CONCLUSIONS

Definite conclusions are not justifiable from a survey of this sort. Several surgeons performed these operations, and the various technics were not represented by equal numbers of cases. The postoperative follow-up period varied from three to 18 months. The severity of the condition and the number of recurrences were not equally distributed for the various operative procedures. Many patients were subjected to the same exciting factors after operation, whereas others were not. However, certain observations may be of value.

Every pterygium should be removed surgically; and the earlier the operation, the better will be the functional and cosmetic result. It is important to succed with the first operation, because a recurrence may result in a major ophthalmologic problem. A surgically sound procedure is one of the "bare sclera" methods, which also calls for total removal of the pathological subconjunctival tissues. This may be accomplished by the methods advocated by D'Ombrain, Sugar, McGavic or me. An operation which diverts the direction of the blood vessels after excision of the growth also seems to be attended with higher success. We prefer to combine these two procedures by performing a Campodónico (figure, *J* and *K*) or a Bangerter (figure, *L*, *M* and *N*) operation, at the same time leaving a small area of bare sclera 1 to 2 mm. in width at the limbus. Although these methods are recommended in the majority of cases of pterygium, including the recurrent type, no one technic should be used in all cases. It is better to make the operation fit the pterygium rather than the pterygium fit the operation. In other words, the procedure should be varied, depending on the type of the lesion and the stage of growth. The early pterygiums are well treated by Campodónico's method. Bangerter's technic is useful for larger growths. Multiple recurrences are best treated by a "bare sclera" method, a mucous membrane transplant or Spaeth's rotating island flap. Roentgen therapy after operation may aid in preventing further recurrence; however, it was not definitely effective in our experience. Beta radiation may eventually prove to be of great value for this purpose when it becomes more widely available.

49. Goar, E. L.: Handbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1948, p. 80.

ADHERENCE SYNDROME

Pseudoparalysis of the Lateral or Superior Rectus Muscles

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ADHERENCE of the lateral rectus to the insertion of the inferior oblique muscle has been observed by many surgeons. After my demonstration of such an adherence at the 1946 meeting of the American College of Surgeons, in Cleveland, Dr. Bruce Fralick expressed it as his opinion that such an adherence might be postinflammatory, a view also expressed by Dr. Virgil Casten and Dr. Albert Ruedemann. Dr. Walter H. Fink[1] appears to have made the only recorded mention of this anomaly, when he stated:

> . . . In addition to the above [the insertion of the inferior oblique was unusually long and surrounded the optic nerve], it seems advisable to mention that on two occasions during operation, a fusion of the inferior oblique and the lateral rectus was noted. This anomaly apparently attributed [sic] to the unusual type of strabismus noted in the patient pre-operatively. Whitnall did not note any anomalies in the attachment of this muscle.

The relation and extensions of the sheaths of the extraocular muscles have been studied intensively in the past few years. Berke described the sheaths of the superior oblique. Scobee emphasized the importance of check ligaments, "foot plates" and strabismus fixus and their surgical significance. The present discussion introduces the "fixed muscle" duction test, which not only makes possible a preoperative diagnosis of adherent rectus muscle, for the muscles to be operated on, but enables one to test muscles not scheduled for operation. Employment of the "fixed muscle" test has also demonstrated the presence of adherence between the superior rectus muscle and the insertion of the superior oblique muscle, a condition, to my knowledge, not previously described.[2]

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1. Fink, W. H.: A Study of the Anatomical Variations in the Attachment of the Oblique Muscles of the Eyeball, Tr. Am. Acad. Ophth. **51**:500-513 (May-June) 1947.

2. Except as shown by moving pictures to a selected group attending the 1949 meeting of the Association for Research in Ophthalmology in Philadelphia.

As will be shown later, this adherence is considered a manifestation of faulty development into the loose, physiological attachments, as described by Fink, and is found frequently in persons younger than 3 years of age, occasionally at the age of 3 to 5 years and seldom after the age of 5 years. Adherence of the lateral rectus to the inferior oblique muscle has been seen as an etiological factor in the production of strabismus simulating bilateral lateral rectus paralysis in three of five children, the father of whom had a strabismus in infancy which "straightened by itself" at the age of about 6 years. A further suggestion of congenital delayed development is found in the observation that when this adherent area has been separated by external lysis (without opening the conjunctiva) the infant obtains normal lateral rotation without evidence of reformation of the adherence.

Since adherence of the lateral rectus to the inferior oblique muscle near the insertion of the latter necessarily limits external rotation, this

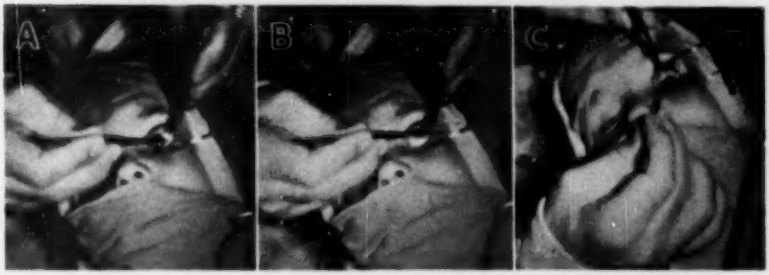

Fig. 1.—Preoperative "fixed muscle" duction test. (*A*) With muscle fixed (forceps in the left hand), forced duction of the globe with forceps in the right hand (applied at the limbus) should be unrestricted, allowing 30 to 45 degrees of lateral forced rotation. This unrestricted relation between the sheaths of the lateral rectus and inferior oblique muscles exists in all eyes in which voluntary external rotation is present, and in eyes with true nuclear paralysis of the sixth nerve.

(*B*) Many infants with supposed lateral rectus paralysis (frequently bilateral) have adherence of the sheaths of the lateral rectus and inferior oblique muscles which prevents forced "fixed muscle" duction. This adherence allows only about 20 degrees of forced rotation, even with exertion of considerable force. Lysis of the adhesion allows complete voluntary external rotation, disproving by surgical means the preoperative appearance of nuclear paralysis of the sixth nerve.

(*C*) Appearance of superior rectus paralysis with overaction of the contralateral inferior oblique muscle will frequently be found to be due to adherence of the sheaths of the superior rectus and superior oblique muscles. The "fixed muscle" duction test should be made before impairing the function of the inferior oblique, since even very loose adherence can cause disparity in elevation of the two eyes. Forcible "fixed muscle" duction frequently lyses this loose adherence without the necessity of exposing the muscle.

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and, again, to a similar group during the 1949 meeting of the American Academy of Ophthalmology and Otolaryngology, in Chicago.

syndrome could not occur in the normal eye or in that strabismus in which external rotation is not limited. The first criterion for the suspected presence of adherence of the lateral rectus and inferior oblique sheaths must, therefore, be the clinical appearance of paresis of the lateral rectus.[3] If external rotation is limited, there may be true paresis or there may be adherence, and the "fixed muscle" duction test (fig. 1 *A*, *B* and *C*) must be employed for further understanding. If external rotation is normal, the presence of physiological, loose union follows the descriptions of anatomic dissections by Fink. If external rotation is limited and adherence is found surgically to be increased, and if the lysis of this area of adherence increases lateral rotation, only then is the etiological diagnosis of adherent lateral rectus syndrome possible.

A postinflammatory cause of function-preventing adherence would scarcely follow this age distribution and should not cause such generally

Four Variations of the Adherence Syndrome

Anomaly	Clinical Appearance
1. Lateral rectus adherent to inferior oblique at their crossing	Lateral rectus paresis or paralysis (usually bilateral)
2. Lateral rectus adherent to inferior oblique with inferior oblique carried forward toward lateral rectus insertion (theoretically possible; has not been seen)	Theoretically, simulation of paralysis of inferior oblique (The thick, tendinous "check ligament" occasionally seen extending from the lower border of the lateral rectus sheath to the inferior oblique, without apparent significance, might be an adherent sheath, having been embryologically carried forward with the developing lateral rectus muscle)
3. Superior rectus adherent to superior oblique at its normal crossing near the insertion of the superior oblique	Simulation of paresis of superior rectus (usually with overaction of opposite inferior oblique)
4. Superior rectus adherent to superior oblique with superior oblique carried forward toward superior rectus insertion	Simulation of paralysis of superior oblique with head tilting

bilateral adhesions. Neither would a postinflammatory cause account for the frequent presence of adherence of both lateral rectus and both superior rectus muscles in children with a condition diagnosed as bilateral external rectus paralysis and bilateral superior rectus paralysis with overaction of the opposite inferior oblique.

Theoretically, there are four possible variants (table) of the adherence syndrome. Three have been seen surgically, and, in fact, photo-

3. For several years I employed the term pseudoparalysis of the lateral rectus in relation to those children for whom a preoperative diagnosis of lateral rectus paralysis had been made and in whom it was found, after resection of the lateral rectus, that the paresis or paralysis no longer existed. It was in one of these infants, in 1942, that I first observed that the stump could not easily be externally rotated to the resection position on the muscle (for tying the suture) until after the adherent tissue had been separated. Repeated observation on this adherence caused me to abandon the term pseudoparalysis in favor of the etiological explanation—adherent lateral rectus syndrome.

graphs from moving pictures illustrate each of these three conditions (figs. 2 to 4). The fourth possible variant may be found to be present; however, I should predict that it must be very infrequent.

ADHERENCE OF LATERAL RECTUS TO INFERIOR OBLIQUE AT THEIR CROSSING

Notwithstanding the presence of definite reflections from the sheath of the lateral rectus onto the sheath of the inferior oblique, and even extending onto the optic nerve, this relationship is normally physiologi-

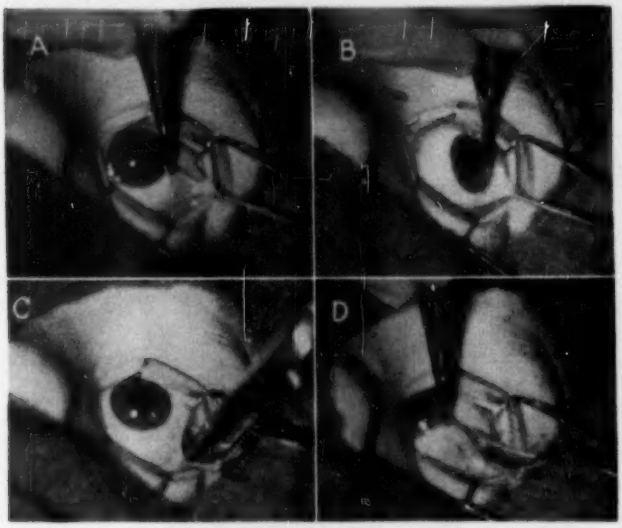

Fig. 2.—(*A* and *B*) External, or closed, lysis. (*A*) "Fixed muscle" duction, if sufficiently forcible to lyse the adherence, allows normal voluntary lateral rotation. Especially is this useful for the side opposite that of operation, or for infants who are emmetropic or myopic with pseudoparalysis, but who have little, if any, squint in the primary position.

(*B*) Adherence is sufficiently weak to allow separation without tearing of the conjunctiva at the limbus. If adherence is too strong, it is necessary to expose the area and treat it directly by open lysis.

(*C*) Demonstration of adherence by probing or by direct observation. Normal loose reflection of the sheaths of the lateral rectus and inferior oblique muscles present almost no resistance to the passing of scissors or a squint hook between these muscle sheaths.

(*D*) Open lysis. Adherent sheaths of the lateral rectus and inferior oblique muscles can almost always be lysed by forcibly rotating the globe against the fixed muscle.

cally loose. While this loose reflection was definite enough to be described by Fink, there was not sufficient adherence to limit rotation. In the

adherence syndrome, rotation is limited because the functional attachment of the lateral rectus becomes that attachment of the inferior oblique which is so far posterior that even powerful efforts at lateral rotation could not rotate externally, but could only retract, the temporal aspect of the globe. Preoperative demonstration of the adherence is easily made by grasping through the conjunctiva the lateral rectus muscle with one pair of toothed forceps (much as one would grasp the superior rectus muscle for inserting a bridle suture) and, with the other forceps, grasping the stump of the lateral rectus muscle or the conjunctiva near the limbus.

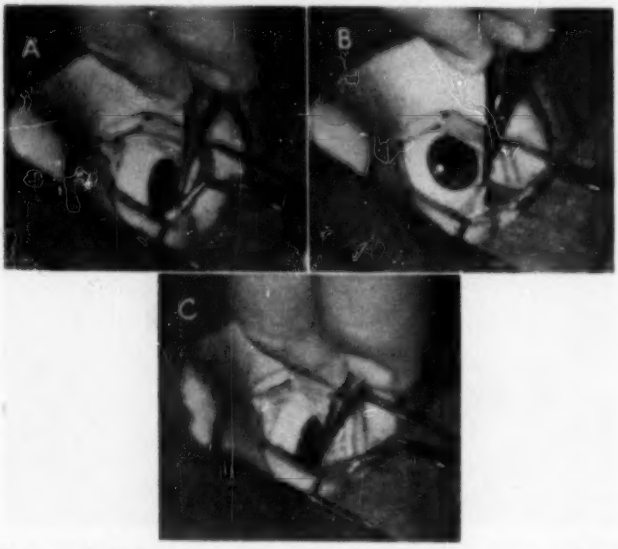

Fig. 3.—(*A*) There is no resistance to internal rotation, nor is there any resistance to lateral forced duction if the lateral rectus is not fixed but allowed to be carried back with the adherent area.

(*B*) "Fixed muscle" duction test. If the lateral rectus is "fixed" by traction or with the forceps, the eye cannot be externally rotated, the adherence resisting gentle forced duction.

(*C*) Open lysis. Forced duction against the exposed muscle, sufficiently strong to lyse the adherence, is used prior to resection or when adherence is too firm to prevent external (closed) lysis. The separation of such adherent tissue allows postoperative voluntary external rotation.

The normal physiological relationship of the lateral rectus and the inferior oblique muscle should allow about 30 degrees of forced rotation between the forceps. Even a fairly weak adherence will prevent more than a few degrees of forced rotation laterally, and it is advised that this

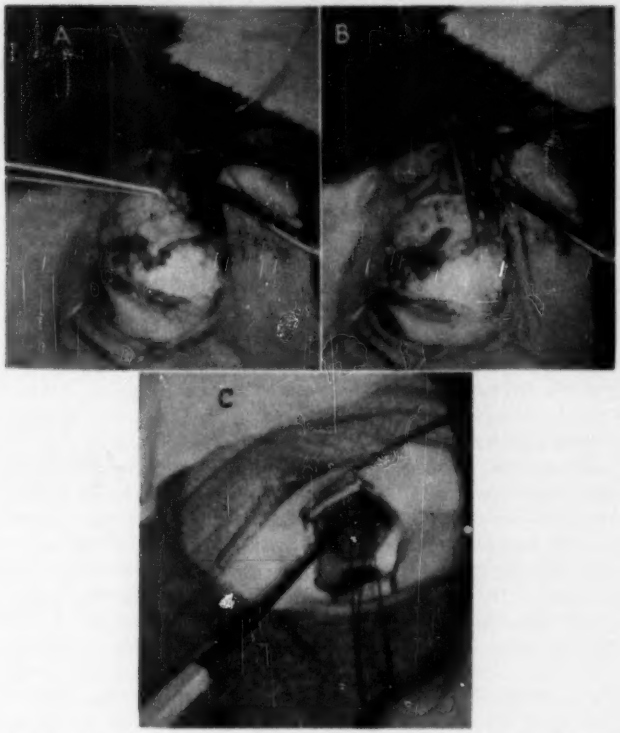

Fig. 4.—(*A* and *B*) Exposure of adherence of the superior rectus and superior oblique muscles.

(*A*) The upper pair of forceps exerts gentle traction on the superior rectus tendon. The lower forceps is on the anterior edge of the abnormally wide, muscular, rather than tendinous, superior oblique. Note the complete adherence of these two muscles. The eye is depressed for photographic exposure by traction on the suture in the stump of the superior rectus.

(*B*) Open lysis is almost completed. The forceps at the upper right is on the superior rectus tendon; the forceps at the upper left is on the anterior edge of the obviously wide, muscular superior oblique. The eye is depressed for photographic exposure. Lysis of the adherent area allows voluntary elevation of the globe and relief from the appearance of an overactive inferior oblique of the opposite eye.

(*C*) Adherence syndrome of the superior rectus and superior oblique with the superior oblique carried forward to a point near the insertion of the superior rectus.

A suture has been placed in the stump to depress the globe for photographic exposure. A suture in the superior rectus tendon maintains normal relations to the stump. A squint hook is passed under the normally tendinous, but anteriorly displaced, superior oblique tendon. Note that the superior oblique muscle bends sharply back from the point of adherence, to course under the superior rectus muscle and insert at its normal location. The appearance of paralysis of the superior oblique with head tilting was completely relieved without operation on the superior oblique other than lysis of the adherence.

"fixed muscle" duction test be done prior to operation on all patients with the appearance of lateral rectus paralysis. If definite resistance is encountered, the muscle is exposed and severed from the stump with the muscle clamp secured to the muscle. The area of adherence may then be directly examined by forcible internal rotation of the globe, especially if a hook is placed under the inferior oblique so that the adherent area may be drawn forward and viewed directly. Even a moderately firm adherence may be separated by holding taut the lateral rectus with the muscle clamp and forcibly rotating the globe externally with the forceps grasping the cut stump (open lysis). Only occasionally is the adherence so firm that it is necessary actually to cut the tissue between the two muscle sheaths. In cutting, extreme caution must be taken to prevent severance of the inferior oblique muscle, which I have seen done on two occasions. When such firm union is present as to prevent any line for dissection, it is possible to place a suture in the inferior oblique muscle below the crossing of the lateral rectus and to cut off the inferior oblique below the lateral rectus in its normal lineal relationship. This has not resulted in any limitation in action of the inferior oblique. The first three procedures considered in this paragraph have been recorded on kodachrome® motion picture film, namely, the "fixed muscle" duction test for the presence of a normal relation or of adherence, demonstration of adherence by probing under the taut exposed muscle and visual examination of the adherent area by forcible internal rotation and placement of a muscle hook around the tendon of the inferior oblique. Also recorded are the demonstration of external (closed) lysis (outside the conjunctiva), which should be attempted on the eye not to be operated on; internal (open) lysis before resection, by holding taut the muscle by the clamp and forcibly rotating the globe externally against the traction of the muscle stump, and section of an adherence so firm as to resist separation by traction or blunt dissection.

The diagnosis of adherent lateral rectus muscle has important surgical significance. It is a frequent procedure to increase the estimated correction for strabismus when a diagnosis of lateral rectus paralysis is made. When the limitation of abduction has been shown to be due to adherence, and not to true paresis, and when this adherence can be freed, the above increase should not be added, or the result will be overcorrection.

ADHERENCE OF SUPERIOR RECTUS TO SUPERIOR OBLIQUE AT NORMAL CROSSING OF SUPERIOR RECTUS NEAR INSERTION OF SUPERIOR OBLIQUE

In the superior rectus adherence syndrome, elevation of the globe is limited because the functional attachment of the superior rectus becomes that attachment of the superior oblique so far posterior that even powerful efforts at elevation could not elevate the globe, but could retract

only slightly the posterior pole. Isolated adherence of the superior rectus to the superior oblique is occasionally found, but this adherence is usually seen accompanying adherence of the lateral rectus to the inferior oblique. The clinical appearance is that of paresis of the adherent superior rectus, with overaction of the opposite inferior oblique. This is demonstrated most obviously when there is a clinical diagnosis of bilateral rectus paralysis, with overaction of one or both inferior oblique muscles. Here the true etiologic factor frequently is adherence of the lateral rectus muscles of both eyes to the inferior oblique muscles, and also adherence of one or both superior rectus muscles to the corresponding superior oblique muscles. Of great surgical importance is the finding of adherence between the superior rectus and the superior oblique muscle, because the best functional result follows lysis of this adherence, rather than a procedure designed to weaken the opposite inferior oblique. It frequently happens that the firmest superior rectus adherence is in the same eye as the firmest lateral rectus adherence, and it is surgically convenient to obtain lysis of these two rectus muscles in one eye, accompanying the resection and recession, so that under one eyepad one has corrected the proper degree of squint and has permitted lateral rotation and upward rotation, with prevention of the appearance of overaction of the opposite inferior oblique muscle. Frequently, external lysis (separation of the adherent area by grasping the muscle at the equator with one forceps and the stump of the rectus with another, and then approximating the two forceps, as is done in testing) is sufficient for the eye with the smaller amount of adherence; and, of course, an eyepad is not necessary after external lysis.

ADHERENCE OF SUPERIOR RECTUS TO SUPERIOR OBLIQUE, WITH SUPERIOR OBLIQUE CARRIED FORWARD TOWARD INSERTION OF SUPERIOR RECTUS

This rare anomaly simulates paresis of the superior oblique with head tilting and is easily missed if the relation to the superior rectus is not examined prior to engaging the superior oblique tendon on the squint hook, for an area of disabling adherence may easily be separated in making the exposure. In the few cases of this anomaly which I have seen, the superior oblique was not advanced, but simply separated from the superior rectus and allowed to fall back along the equator to its functioning position, with relief of head tilting and establishment of apparently normal function. Examination of this relationship on exposure shows that the superior oblique tendon has been carried forward almost to the stump of the superior rectus and that it then turns back almost directly under the rectus to attach at its normal stump. Depression of the globe is, of course, impossible with the functional attachment at the retrolimbal attachment of the superior rectus. Of considerable interest is this finding, since it points emphati-

cally to an anomalous developmental factor, the superior oblique having been carried forward with the superior rectus as the latter grew forward.

SUMMARY

Evidence is presented suggesting that anomalous development results in the presence of adherence of the sheaths of the lateral rectus and inferior oblique muscles and that a second form of the adherence syndrome exists because of union between the superior rectus and the tendon sheath of the superior oblique. Presurgical examination with the "fixed muscle" duction test is recommended with all patients having the appearance of lateral rectus paralysis, superior rectus paralysis with overaction of the opposite inferior oblique or superior oblique paralysis with head tilting. Even weak adherence should be freed (open lysis) before one proceeds with the resection sutures, and in case of the bilateral adherence syndrome it is usually possible to free the weaker adherence without opening the conjunctiva by forcible "fixed muscle" duction (closed lysis).

MEDICAL WRITINGS OF DR. HARRY FRIEDENWALD

The contributions which the late Dr. Harry Friedenwald made were numerous and his interests were widespread. The ARCHIVES believes that his medical writings should be listed because of their value to ophthalmology.

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Annual Reviews

GLAUCOMA

A Review of the Literature, 1949-1950

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GLAUCOMA is one of the most baffling diseases in ophthalmology, as well as one of the most serious. The number of papers appearing in the literature on the subject and the divergent views expressed therein confirm the unsolved nature of the condition. This is particularly distressing because the treatment must of necessity be empirical as long as the underlying disturbances in physiology remain obscure. This review attempts to cover, as nearly as possible, the pertinent available papers published during the past year and to organize them into various categories under which the disease might be considered.

I. PRIMARY GLAUCOMA

A. Mechanism.—Two main schools of thought regarding the mechanism of origin of primary glaucoma today are widely accepted. One school believes that all primary glaucoma arises from a disturbance in the ocular-neurovascular system, whereas the other considers primary glaucoma chiefly from a mechanical point of view. Speculation has always been keen as to the cause of glaucoma, but interest in the subject has been greatly stimulated during the past year, particularly in this country, as a result of recent papers by Duke-Elder.[1] He favors a neurovascular disturbance as the underlying factor in all types of primary glaucoma, more or less to the exclusion of present day mechanical concepts.

1. Neurovascular Disturbance: Duke-Elder takes issue with the gonioscopic classification advanced by the symposium on glaucoma presented at the annual meeting of the American Academy of Ophthalmology and Otolaryngology in 1948. He believes, instead, that glaucoma should be divided into two categories, congestive and noncongestive.

He considers congestive glaucoma to be due fundamentally to a vascular instability, which, during acute stages, results in vasodilatation,

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1. Duke-Elder, S.: The Dependence of Surgery on Physiology, with Special Reference to the Treatment of Glaucoma, Am. J. Ophth. **33**:11, 1950; Fundamental Concepts in Glaucoma, Arch. Ophth. **42**:538 (Nov.) 1949; The Physiology of the Intraocular Fluids and Its Clinical Significance, Am. J. Ophth. **32**:1638, 1949.

increased capillary permeability and edema. This entire process is accentuated by means of axon reflexes. These acute episodes are probably precipitated by factors as yet undetermined, such as neurohumoral anomalies, upsets in the balance between the sympathetic and the parasympathetic nervous system and endocrine dyscrasias. Other factors, physical or psychosomatic, such as those stemming from emotional upsets involving the thalamus and hypothalamic region have been suggested. More specific precipitating factors are found in instances in which congestive glaucoma follows certain inflammatory lesions of the eye, trauma to the eye, irritation of a dislocated lens, venous obstruction or other disorders. Regardless of these factors, Duke-Elder believes that the local pathologic condition is clear, consisting of capillary dilatation, increased permeability, stasis and local edema, and often increased intraocular pressure. He states that congestion and edematous swelling of the ciliary body may force the iris against the cornea. If this is repeated a sufficient number of times, increasing numbers of peripheral anterior synechias may form. He therefore believes that the depth of the angle is not a factor in precipitating the chain of events which he describes, but is only the result of such vascular crises. Likewise, the elevated tension is a secondary consideration.

Duke-Elder also attributes noncongestive, or chronic simple, glaucoma to a somewhat different vascular disturbance from that which produces the acute type. This consists of an instability of vascular control over the intraocular circulation which is characterized by insufficient nutrition of the ocular tissues, causing subsequent sclerosis and atrophy, rather than stasis or edema, such as is found in the congestive variety. Duke-Elder describes three manifestations of this circulatory disturbance, in which he attempts to explain the origin of low tension glaucoma, as well as those types in which the tension is rather high early in the disease. 1. If the vessels of the posterior segment of the eye are involved, either alone or out of proportion to the involvement of the vessels of the anterior portion of the eye, nutritional excavation of the nerve head occurs, even though the ocular tension is within normal limits. The picture of glaucoma without elevation of tension therefore results. The excavation of the nerve head, he assumes, is due to lacunar atrophy, which results from sclerosis of the nutrient vessels of the optic nerve. 2. If the vessels of the anterior segment are particularly affected, a rise in tension is an early feature of the disease, and the changes in the optic nerve occur late. In this case, he believes that the glaucoma results from an interference with drainage of fluid from the eye, probably because of sclerosis of the vessels of the anterior segment. 3. If the vascular involvement affects the whole eye and is associated with the sclerotic effects which Duke-Elder postulates, the typical picture of glaucoma simplex with increased tension occurs.

Duke-Elder cites certain supporting evidence in presenting his lucid arguments. He mentions a significant number of patients with glaucoma who have a general vascular instability, reflected both in the systemic blood pressure and in the local responses to various stimuli. He also cites the importance of emotional factors involved in such disturbances.

As evidence along the same line, but signifying instability of the ocular system of vessels, he emphasizes that early in its course chronic simple glaucoma is manifest not so much by a rise in tension as by distortion and exaggeration of the normal diurnal tension curve. This he believes is due to rhythmic circulatory changes. The base pressure may remain unelevated, but the variations in tension are greater than normal. As further corollary evidence, he mentions the difference in the local vascular state during the phases of high and low tension. For example, fluorescein permeability tests indicate a great variation in capillary permeability. For normal eyes a standard curve is found, whereas in glaucomatous eyes the permeability is usually much greater and there are sudden, unexpected variations. He also states that lability tests and venous pressure tests are usually positive during the phases of ascending tension of the diurnal curve in these glaucomatous eyes but are negative in the descending phase. These findings, he says, indicate lack of capillary stability during the phase of rising tension, a condition which does not exist during the descending phase.

Numerous other articles have been written in support of the neurovascular, neurovegetative theory of the origin of glaucoma during the past year. Filbry [2] suggests that chronic simple glaucoma may result from a constitutional hypofunction of the parasympathetic nervous system. This suggestion was supported by his finding that the ocular tension of several patients responded favorably to local or subcutaneous administration of acetylcholine. In my opinion, this observation might be questioned, because acetylcholine is ordinarily destroyed so rapidly in the tissues that when dropped into the eye it is incapable of producing miosis. As an observation along the same line, Jaffe [3] showed that sympathectomy was followed by some lowering of the intraocular pressure of cats, although he hesitates to draw any conclusions regarding the exact role of the sympathetic system in glaucoma. Pau [4] states that he believes primary glaucoma is due to a hypertonicity of the sympathetic system, a condition resulting from a disturbance in the com-

2. Filbry, E.: Zur Aetiologie und Genese des Glaukoma simplex, Klin. Monatsbl. f. Augenh. **115**:506, 1949.

3. Jaffe, N. S.: Sympathetic Nervous System and Intraocular Pressure, Am. J. Ophth. **31**:1597, 1948.

4. Pau, H.: Das Primärglaukom als Tonusherabsetzung im Ziliarmuskel infolge bestehender Sympathikotonie, Klin. Monatsbl. f. Augenh. **115**:513, 1949.

mon regulating mechanism controlling variations in intraocular tension as well as the systemic blood pressure. He cites the increased frequency of glaucoma in early spring and in winter in support of this theory. He explains this by postulating an increased aran content of the air during winter and spring, aran being a polyvalent oxygen which acts as a stimulant on the parasympathetic nervous system. Godtfredsen [5] observed three patients with Ménière's disease, all of whom had congestive glaucoma. He offers this observation in support of the neurovascular theory, stating that both diseases are due to a neurovegetative disturbance, probably angioneurotic in nature.

Magitot [6] has long favored the neurovascular theory of origin of glaucoma, assuming that the basic disturbance lies in the diencephalon, where he postulates a regulating center for ocular tension is located. In a recent article, he offers experimental evidence, based on determinations of acetylcholine and cholinesterase in the aqueous, to show that a disturbance in this center might result in a deficiency of the parasympathetic system. Schmerl and Steinberg [7] report further observations based on studies of their own along the same lines. In earlier papers they had postulated that the diencephalon acts as a center for control of the intraocular pressure in relationship with the posterior lobe of the pituitary, the latter producing two active principles, one of which causes an increase, and in the other a decrease, in intraocular pressure. They felt that these active principles are secreted into the spinal fluid and carried by it to reach the diencephalic region, to exert their effect on intraocular pressure. The diencephalon, in turn, exerts its effect on intraocular pressure through the medium of the autonomic nerve fibers which supply the eyeball and their effect on capillary action. The present report of these authors is concerned with a study of the effect of the autonomic nervous system on intraocular pressure. They conducted experiments in which the ciliary and cervical sympathetic ganglions were either stimulated or destroyed. Stimulation of the ciliary ganglion resulted in immediate increases of intraocular pressure of from 8 to 17 mm. of mercury. Destruction of the ciliary ganglion by cautery in rabbits resulted in a decrease of intraocular pressure, varying from 8 to 13 mm. of mercury. In such animals, the injection of 40 cc. of distilled water per kilogram of body weight produced little or no change in intraocular tension. In the eyes of normal rabbits the tension rose in such circumstances.

5. Godtfredsen, E.: Concurrence of Glaucoma and Ménière's Disease, Acta oto-laryng. **37**:533, 1949.

6. Magitot, A.: Tension oculaire et diencéphale, Arch. d'opht. **9**:463, 1949.

7. Schmerl, E., and Steinberg, B.: The Role of Ciliary and Superior Cervical Ganglia in Ocular Tension, Am. J. Ophth. **32**:947, 1949.

In previous experiments, they had found that placing rabbits in the dark caused the posterior lobe of the pituitary to liberate a substance into the spinal fluid which stimulated the sympathetic pathway and lowered intraocular pressure. On the other hand, when the animals were exposed to light, a substance was liberated which stimulated the parasympathetic pathways and caused an elevation in pressure. Such effects could be obtained by the intravenous injection of spinal fluid from these animals into others of the same species. After cauterization of the ciliary ganglion, the intravenous injection of spinal fluid from rabbits kept in the dark caused the usual reduction in pressure, but with the use of spinal fluid from animals exposed to light no change in pressure occurred. These investigators concluded, therefore, that removal of the parasympathetic pathways results in failure to transmit those stimuli which cause an increase in tension, but the principle which lowers intraocular pressure by stimulating the sympathetic pathways remains effective.

The reverse was true after sympathectomy. Stimulation of the superior cervical ganglion caused a lowering of intraocular pressure of from 7 to 11 mm. of mercury in normal rabbits. Injections of spinal fluid into such animals from rabbits exposed to light caused an increase in tension of from 3 to 9 mm. of mercury. Injections of spinal fluid from rabbits kept in the dark caused no change, indicating that removal of the sympathetic pathway resulted in failure to transmit those stimuli which caused a decrease in tension. There was no indication that it was interference with the active principle which caused an increase in tension. This work is extremely interesting and will undoubtedly be carried further.

Other papers have appeared which offer additional evidence to relate glaucoma more closely to disturbances of the general vascular system. Diensthier and associates[8] found that vascular hypertension was much more frequent in patients with glaucoma. Congestive glaucoma was often associated with paresthesias of the limbs, cyanosis, intermittent claudication, migraine, hypertension and varicose veins. Oscillotonometric tests revealed a decreased oscillatory index in cases of primary glaucoma, particularly the chronic simple type, whereas these tests gave a normal index with secondary glaucoma. This observation would support a vascular disturbance as the cause of primary glaucoma. These investigators also studied capillary function and found evidence of vasoneurosis in patients with congestive glaucoma, whereas relation to arteriosclerosis was found in patients with chronic simple glaucoma. Such objective studies must certainly be given considerable weight.

8. Diensthier, E.; Balik, J., and Kafka, H.: A Contribution to the Theory of the Vascular Origin of Glaucoma, Brit. J. Ophth. **34**:47, 1950.

Haselmann[9] attempted to approach the problem through laboratory methods, consisting of determinations of the basal metabolic rate, blood cholesterol and blood sugar tolerance, urinary concentration and dilution tests and roentgenographic studies of the skull. He found a tendency to elevation of the basal metabolic rate and a disturbance in blood sugar tolerance curves, but it was the impression that no conclusions could be drawn. The author feels that at best his results may indicate an endocrine disturbance. Cristini[10] attempted to show a relationship between the cardioaortic and the sinucarotid reflexes in patients with primary glaucoma, but the evidence was not very conclusive. Brückner and associates[11] showed that the ocular tension tended to be higher as the patient's head was lowered, a finding which was not influenced by the previous topical application of physostigmine or neostigmine. The elevation, however, could be suppressed by the instillation of atropine. It would seem that the factors involved in their studies were based to some extent on the same principles as provocative tests which involve interference with venous return from the head region.

Matteucci,[12] in an interesting paper, reports that glaucoma without ocular hypertension was frequently seen with permanent arterial hypotension. He suggests that treatment be directed against the latter. He states that, in his opinion congestive glaucoma of both the acute and the chronic type was most frequently seen in association with paroxysmal arterial hypotension, which occurs secondary to such conditions as cardiopathies, infectious disease, endocrine disorders and sinucarotid hypersensibility. He states that glaucoma appears during the crisis of hypotension. Matteucci's claims seem to have little basis for support in the literature.

Duke-Elder, however, states that the cause of glaucoma is still unproved and that the problem is left for future investigations, many present day ideas being somewhat philosophical.

2. Mechanical Theory: The mechanical theory of origin of glaucoma had its inception in 1923, when Raeder found that acute congestive glaucoma was associated with a shallow anterior chamber whereas the chronic simple type was more generally associated with a chamber of normal depth. Since that time considerable evidence has been accumulated by

9. Haselmann, G.: Untersuchungen zur Frage Glaukom und Allgemeinstörungen, Klin. Monatsbl. f. Augenh. **118**:527, 1949.

10. Cristini, G.: Reflettività cardio-aortica e sinu-carotidea nei glaucomatosi primari, Giorn. ital. oftal. **1**:385, 1948.

11. Brückner, R.; Hermann, C., and Jent-Peyer, S.: Beitrag zur physikalischen und pharmakologischen Beeinflussung des Augendruckes, Ophthalmologica **118**:520, 1949.

12. Matteucci, P.: Les glaucomes des hypotendus artériels, Ann. d'ocul. **183**:313, 1950.

many investigators through anatomic and gonioscopic studies to show that congestive glaucoma characteristically occurs in eyes with narrow angles, whereas in a majority of instances chronic simple glaucoma occurs in eyes with angles of normal width. The accumulated evidence led the committee presenting the symposium on primary glaucoma at the American Academy of Ophthalmology and Otolaryngology (1948) to adopt the gonioscopic classification. Most authors of papers on glaucoma appearing in this country during the past year have accepted these gonioscopic concepts, although no particularly outstanding contributions to their support have been made during this time.

Several papers have appeared on the subject of aqueous veins, a phase of ocular anatomy and physiology which may prove to favor either the mechanical or the neurovascular theory. Interest in these vessels has developed rapidly since their description by Ascher, and as a result of subsequent work, particularly by Ascher and Goldmann. Ascher has suggested that obstruction to the aqueous veins, such as might follow extensive surgical procedures on the anterior segment, might be a factor in causing elevated ocular tension. Goldmann, on the other hand, after studying the behavior of aqueous veins, suggested that the high incidence of the negative glass rod phenomenon in chronic simple glaucoma (filling of the aqueous veins with blood, coincident with pressure on the recipient vessel) might signify an increased filtering resistance between the anterior chamber and the canal of Schlemm, with resultant low pressure in the aqueous veins. Ascher [13] suggests that since blood flows back into the aqueous veins on pressure (negative glass rod phenomenon), but not into the canal of Schlemm, the outlets of the canal into the aqueous veins may instead be narrowed.

Gaba [14] takes exception to Goldmann's theory because he feels that the pressure within the episcleral veins, as well as the effects of pressure on them, must be taken into consideration. He feels that large differences of pressure within these vessels might result from very small changes in caliber due to external pressure. Therefore pressure with a glass rod in eliciting the glass rod phenomenon might of itself alter the direction of aqueous flow in the veins, a phenomenon possibly not related to differences of pressure in the canal of Schlemm. Such objections are difficult to refute. Goldmann [15] attempted to analyze the circulation of aqueous through the canal of Schlemm and into the

13. Ascher, K. W.: Aqueous Veins and Their Significance for Pathogenesis of Glaucoma, Arch. Ophth. **42**:66 (July) 1949.

14. Gaba, V.: A Criticism of Goldmann's Interpretation of Ascher's Phenomenon, Ceskoslov. oft. **5**:168, 1949.

15. Goldmann, H.: Die Kammerwasservenen und das Poiseuille'sche Gesetz, Ophthalmologica **118**:496, 1949; Zur Frage der Sitzes der Widerstandserhöhung beim einfachen Glaukom, ibid. **119**:267, 1950.

aqueous veins by mathematical means, but his figures might be questioned because of the lack of any actual measurements of many of the essential factors, such as minute volume of aqueous elimination and the viscosity of the contents of the vessels. He attempted to correlate outflow readings with gonioscopic changes in three cases of glaucoma, again without very conclusive results.

The phenomenon observed in aqueous veins has been adopted by the proponents of the neurovascular theory of origin of glaucoma, as well as by the advocates of the mechanical school of thought. Thomassen [16] believes that the glass rod phenomenon is directly related to the level of pressure within the episcleral veins, into which the aqueous veins drain. Thomassen adopts the premise that the venous pressure is high in proportion to the intraocular pressure when the intraocular pressure is in an increasing phase and that it is lower when the intraocular pressure is in a decreasing phase. He found that the glass rod phenomenon was negative during periods of increasing ocular tension, whereas in the same eyes and the same veins it was positive during periods of decreasing tension. As a result, the aqueous displaces the blood from the recipient veins during the decreasing phase, when the venous pressure is lower, and the reverse occurs during periods of rising tension. To him this observation refutes Goldmann's idea that the glass rod phenomenon is negative in glaucomatous eyes because of low pressure in the aqueous veins resulting from increased resistance in the permeable membrane between the anterior chamber and Schlemm's canal. He likewise does not accept Ascher's explanation that the glass rod phenomenon is negative as a result of decreased pressure in the aqueous veins through interference with the outflow of blood due to narrowing of the outlets of Schlemm's canal.

All these authors agree that the glass rod phenomenon is usually positive in normal eyes, and that it is consistent for any given vein in repeated tests. In eyes with chronic simple glaucoma the phenomenon tends to be negative, except that the results of the test are not as consistent as in the normal eye or when the pressure has been controlled by miotics or by operation. Thomassen [17] explains the inconsistency in glaucomatous eyes by first indicating that the venous pressure varies as stated above, according to whether the ocular tension is increasing or decreasing. Furthermore, when the tension is elevated, the intraocular venous pressure is considerably higher than the venous pressure outside the eye. A sharp gradient, therefore, must result, which, in turn, leads to the negative glass rod phenomenon.

16. Thomassen, T. L.: The Glass Rod Test in Glaucomatous Eyes, Brit. J. Ophth. **33**:773, 1949.

17. Thomassen, T. L.; Perkins, E. S., and Dobree, J. H.: Aqueous Veins in Glaucomatous Eyes, Brit. J. Ophth. **34**:221, 1950.

Weinstein [18] reports observations somewhat similar to Thomassen's. He compressed the jugular vein, causing Schlemm's canal to fill with blood, and thereby demonstrated that the two systems are in close communication. Somewhat along the lines of Ascher's glass rod test, he showed that on removal of the venous obstruction the striated vessels containing blood and aqueous quickly regained their appearance in normal eyes. The process, however, was greatly delayed in cases of chronic simple glaucoma because of the increased pressure in the efferent vein. The author also observed that on elicitation of a negative glass rod phenomenon the vessels quickly regained their former appearance in normal eyes but that the process was greatly delayed in eyes with chronic simple glaucoma. This, he feels, was due to increased pressure in the efferent vein. This somewhat confirmed Thomassen's work. The author believes that there also are efferent vessels containing aqueous which drain posteriorly through the ciliary system. As evidence of this, he cites the fact that he and Bussaca were unable to find aqueous veins in cases of hydrophthalmos. In spite of that, and assuming that Schlemm's canal was absent or replaced with tissue hyperplasia, the tension stabilized at a moderate height, indicating escape of aqueous. This, he feels, presupposes a drainage system other than that of Schlemm's canal, with its aqueous veins.

Weekers and Prijot [19] report that rabbits and guinea pigs have aqueous veins which are analogous to those of human beings, and they submit their observations on the study of these vessels. They claim to have shown that the pressure in the aqueous veins rises, and likewise falls, according to the pressure within the anterior chamber. If the ocular tension is less than 15 mm. of mercury, the flow of aqueous in the veins is halted.

The differences of opinion between those who hold to the neurovascular theory of origin of glaucoma and those who support the mechanical theory, which is based largely on gonioscopic concepts, are not as profound as they appear. They can be resolved to a large extent, because most ophthalmologists who accept the gonioscopic classification of glaucoma believe that no specific etiologic factor for the disease is implied. Instead, this classification is sufficiently elastic to embrace the various causes of glaucoma as they may be recognized in the future. At the same time, it seems to offer a reasonably satisfactory division of glaucoma into two broad, but distinct, types, based on a fairly consistent appearance

18. Weinstein, P.: New Concepts Regarding Anterior Drainage of the Eye, Brit. J. Ophth. **34**:161, 1950.

19. Weekers, R., and Prijot, E.: Recherches expérimentales sur les fonctions des veines aqueuses, Ophthalmologica **119**:321, 1950.

of the angle of the anterior chamber and a rather typical clinical course. Such a classification seems to offer a practical yet dynamic approach to the study of primary glaucoma.

The neurovascular school adheres to the older terminology of chronic simple, rather than wide angle, glaucoma and to congestive rather than narrow angle, glaucoma. Duke-Elder, however, agrees that the two classifications run quite parallel.

The most irreconcilable difference between the two schools is found in the mechanism of acute congestive (narrow angle) glaucoma. The neurovascular theory assumes that this disease occurs solely on the basis of a neurovascular disturbance which produces edema of the ciliary body, with resultant narrowing of the angle. The width of the angle is therefore only a secondary feature. The mechanical theory assumes such eyes to have anatomically narrow angles, which predispose them to attacks of glaucoma. Acute attacks are thought to occur whenever the angle becomes blocked through any cause which forces the periphery of the iris into contact with the trabecular region of the angle of the anterior chamber. Escape of aqueous is therefore prevented, and the intraocular pressure rises rapidly. This might result from factors which seem purely mechanical, such as pupillary dilatation in a dark room, or from neurovascular factors, such as congestion of the ciliary body caused, for example, by emotional disturbances or minor trauma to the eye. The fact that the tension becomes elevated in a dark room with congestion appearing subsequently suggests that at least in some cases the precipitating factor might be mechanical, owing to obstruction of the angle.

Most workers in the field of glaucoma who follow gonioscopic concepts would disagree with Duke-Elder's statement that 20 per cent of eyes with acute congestive glaucoma have angles that are open on gonioscopic examination, unless the examination is made between attacks. Even between attacks, however, such eyes invariably have extremely narrow angles. One's convictions regarding acute congestive (narrow angle) glaucoma become more firmly fixed after repeatedly observing acute rises in ocular tension following mydriasis in eyes with narrow angles, whereas even the pupils of glaucomatous eyes with angles of normal width can be dilated with impunity.

The fact that a peripheral or complete iridectomy can prevent attacks of acute congestive glaucoma has been used as an argument in favor of the neurovascular theory of origin of glaucoma. It is believed by those who advance this argument that such an iridectomy is curative, through its effect on the neurovascular reflexes of the eye. This is hard to accept when the great extent of the vascular bed of the eye is considered. It seems easier to believe that iridectomy prevents mechanical sealing of the angle by keeping at least a portion of the trabecular area open for escape

of aqueous, thereby preventing sudden complete closure of the angle through circumferential contact between the periphery of the iris and the trabecular area.

The gonioscopic classification of glaucoma breaks down most seriously in wide angle (chronic simple) glaucoma, because a significant percentage of eyes with chronic simple glaucoma do have narrow angles. Duke-Elder states that 40 per cent of the eyes with chronic simple glaucoma have narrow angles, but that figure seems high, and one which would arouse great differences of opinion, at least early in the course of the disease. It is recognized, on the other hand, that, for some reason, during the terminal stages of chronic simple glaucoma the angles tend to become narrower, and finally close, as congestion appears. The apparent paradox of anatomically narrow angles occurring in so-called wide angle (chronic simple) glaucoma can be explained only by assuming that the width of the angle of the anterior chamber is an anatomic characteristic, inherent in the individual. As a result, such an eye, although predisposed to attacks of acute congestive glaucoma, may remain normal throughout life, but at the same time be subject to chronic simple (wide angle) glaucoma or any other ocular disease.

The gonioscopic designation of chronic simple glaucoma as wide angle glaucoma seems admirably suited to serve as a basis for the future study of this disease because it does not imply that any single cause is responsible; instead, it assumes that there may be several. The problem is therefore recognized and left open for future investigation. It seems likely that what is now known as primary glaucoma will eventually be resolved into several different entities, which will then be regarded as additional types of secondary glaucoma. The concept of wide angle glaucoma is sufficiently elastic to permit the consideration of various causes of the disease, such as a neurovascular disturbance involving either the production or the escape of aqueous or more purely mechanical factors. Among these are changes in the trabeculum, at least one variety of which has been described by Reese as due to a cuticular membrane, or disturbances directly within the canal of Schlemm, the afferent or efferent vessels supplying the canal of Schlemm or even the aqueous veins.

The distinctly different behavior of wide angle and narrow angle glaucoma clinically seems to favor the gonioscopic classification. The danger of pupillary dilatation in eyes with narrow angles has been repeatedly observed, whereas there is little danger in dilating the pupils of eyes with normally wide angles. The result of the darkroom mydriasis test is likewise frequently positive in cases of narrow angle glaucoma, while that of the water provocative test is negative. The opposite is true of the wide angle type. Narrow angle, or acute congestive, glaucoma

responds exceedingly well to iridectomy if done early, whereas iridectomy has little effect on the clinical course of wide angle, or chronic simple, glaucoma. Normalization of tension is less certain regardless of the type of operation in eyes with wide angle (chronic simple) glaucoma. Progressive visual deterioration occur rarely after successful surgical treatment of narrow angle (acute congestive) glaucoma, in contrast to the late changes which follow operation in eyes with wide angle (chronic simple) glaucoma, among which are infection, cataract and hypotension. Early operation, therefore, is advised in cases of narrow angle glaucoma, but in the wide angle (chronic simple) type surgical intervention is deferred until there is some sign of visual deterioration or greatly elevated ocular tension. Changes in visual fields rarely occur in acute congestive glaucoma in the absence of prolonged rises in ocular tension or repeated acute attacks. On the other hand, they are characteristic of wide angle (chronic simple) glaucoma and offer the key to intelligent follow-up observation. Glaucomatous excavation of the optic nerve head rarely occurs except in the very late stages of narrow angle (acute congestive) glaucoma, when the ocular tension is at a sustained high level, whereas it is characteristic of wide angle (chronic simple) glaucoma.

There seems to be little real difference of opinion between the neurovascular and the mechanical theory of origin of glaucoma with regard to the importance of ocular tension. Both schools of thought assume that the elevated ocular tension is secondary to the underlying factor in glaucoma, whatever it might be, and neither school belittles the importance of repeated tonometric observations in following the response of the disease to treatment. The neurovascular theory, however, assumes that many of the degenerative ocular changes, such as excavation of the optic nerve, probably result from vascular disease rather than from pressure.

Proponents of the mechanical theory would be more prone to believe that, aside from the underlying cause of glaucoma, whether it be neurovascular or some other, many of the pathologic changes are caused by the elevated intraocular pressure itself. A classic example is found in children with buphthalmos, in which the globe enlarges, as a result of excessive intraocular pressure, until rupture of the eyeball may be imminent. This enlargement ceases if the pressure is normalized surgically. Another example is the rapid onset of optic nerve atrophy and glaucomatous cupping associated with uncontrolled glaucoma following cataract extraction, a type of disease usually due to mechanical obstruction of the angle of the anterior chamber. Still another example is rapid optic nerve atrophy and loss of vision which occur during acute uncontrolled attacks of congestive glaucoma with extremely elevated ocular tension. This can be prevented if the tension is

controlled promptly. They also believe that the rate of onset of glaucomatous cupping and the loss of visual fields in wide angle (chronic simple) glaucoma are likely to be more rapid with high levels of ocular tension than with lower levels. Patients may be treated with miotics for long periods without loss of visual field if the tension ranges between 30 and 35 mm. of mercury; however, few eyes can successfully tolerate ocular tensions over 40 mm. of mercury without the rather rapid occurrence of optic nerve atrophy and progressive visual loss. Glaucoma without hypertension might be offered as an example to refute such statements, but, as Friedenwald has stated, the disease is extremely rare. In our own experience at the Hospital of the University of Pennsylvania, in studying the few such cases which we have seen, the visual loss is usually due to some other cause which simulates glaucoma, such as chiasmal lesions.

Final proof of the cause of primary glaucoma must await further clinical and experimental evidence. The ultimate goal will be reached only when both the terms "wide angle" and "primary" glaucoma are outmoded and each type of glaucoma within the group is identified. The physiopathology of glaucoma is as yet necessarily obscure because not even all the details of the formation of aqueous humor have as yet been elaborated. Notable work is being carried on by Kinsey, Friedenwald, Duke-Elder and others, which is adding greatly to knowledge of the subject, but much remains to be learned. For example, general agreement has only recently been reached that the aqueous humor is at least in part a secretion. New technics are being devised for the study of the physiology of the aqueous, including its formation and circulation, particularly with utilization of tracer substances, which may make clinical observations along the same lines as those previously carried out on animals quite feasible. Cagianut and Verrey[20] already have reported such experiments on human eyes prior to enucleation. They injected heavy water into the anterior chamber and measured its concentration in the aqueous, lens and vitreous following enucleation. They found that half the water was replaced in 2.7 minutes, signifying rapid exchange across the blood-aqueous barrier. A comparison of normal and glaucomatous eyes is not as yet available. The physiology of the aqueous humor is discussed in the October annual review of the ARCHIVES.

B. Perimetric Studies in Glaucoma.—Several articles on perimetric studies in glaucoma have appeared during the past year. Wilson[21]

20. Cagianut, B., and Verrey, F.: Essai de dépistage de metabolisme hydrique dans les milieux transparents de l'oeil humain par injection d'eau lourde dans la chambre antérieure, Ann. d'ocul. **182**:649, 1949.

21. Wilson, R. P.: The Early Diagnosis of Chronic Primary Glaucoma, with Remarks on the Value of Perimetry in Relation to Prognosis and Treatment, Tr. Ophth. Soc. New Zealand **3**:39, 1949.

presents an excellent review and analysis of the subject. The use of small test objects is emphasized. He notes, as was previously pointed out by Traquair, that the so-called Seidel sign does not develop as a direct extension in the blindspot but, instead, begins as a scotoma at a point away from the blindspot, along the distribution of an arcuate scotoma, and only later enlarges and coalesces with the blindspot to produce the appearance of winging. He found depression of the central isopters an early sign of glaucoma, manifest as baring of the blindspot or a Roenne step in the nasal aspect of the central fields, and occurring before there is any obvious irregularity in the peripheral nasal field. These defects can be demonstrated by small white test objects or by larger colored ones. He reemphasized the importance of following the course of glaucoma with measurement of the visual fields, to supplement the periodic recording of ocular tension.

Miles [22] and Weekers and his associates [23] report observations made in studying flicker fusion frequency fields in glaucoma. Miles reports that depression is commoner in the nasal than in the temporal field, and in the peripheral than in the central field, with central loss and baring of the blindspot of 25 of 32 eyes. He found changes in the flicker fusion frequency fields of 24 eyes, in which the ordinary visual fields had been normal, indicating that flicker fusion frequency is reduced before form vision is lost. Weekers and his associates drew similar conclusions as to the sensitivity of the test. They emphasized that the flicker fusion frequency fields are very easy to determine. From these reports, this technic seems to offer an excellent new approach to the early diagnosis and study of glaucoma. Tikhomirov and Siedlovskaya [24] studied changes occurring in the blindspot of normal and of glaucomatous eyes during water provocative tests. They found no changes occurred in normal eyes, but that the blindspot increased in size in all the glaucomatous eyes. They believe that the changes in the size of the blindspot are due to retinal edema or increased permeability of the retinal blood vessels.

C. Medical Treatment of Primary Glaucoma.—No great strides have been made in the medical management of primary glaucoma during the past year. Most of the papers written simply represent attempts to evaluate further the therapeutic measures already available. Christensen

22. Miles, P. W.: Flicker Fusion Fields: Findings in Early Glaucoma, Arch. Ophth. **43**:661 (April) 1950.

23. Weekers, R.; Roussel, F., and Heintz, A.: Les modifications de la fréquence critique de fusion dans le glaucome, Ophthalmologica **118**:555, 1949.

24. Tikhomirov, P., and Siedlovskaya, E.: Increase in the Size of the Blindspot Following the Administration of Water as a New Method of Early Diagnosis of Glaucoma, Vestnik oftal. **28**:23, 1949.

and Swan,[25] in 1948, reported that dibenamine® (N,N,-dibenzoyl-β-chloroethylamine hydrochloride), an adrenergic-blocking agent, was effective in lowering the ocular tension during attacks of acute congestive glaucoma. Its effect, however, was only temporary. Bloomfield and Haimovici [26] report its use in the treatment of chronic simple glaucoma, on the assumption that excessive sympathetic stimulation might be the cause of this disease. They observed its effect on 18 eyes in 9 patients and noted an appreciable fall in ocular tension, beginning within two to three hours after administration of the drug and persisting for periods of 24 to 48 hours. The tension then gradually rose. The authors feel however, that the clinical value of dibenamine® is limited because intravenous administration is required and it produces a rather pronounced postural hypotension. Further study of this new substance is necessary. In our own experience at the Hospital of the University of Pennsylvania it has given more erratic results than those reported by Christensen and Swan and Bloomfield.

Ehlers,[27] Gallino and Bottini,[28] Goedbloed,[29] Raiford,[30] Stone,[31] Vanysek,[32] Wheeler [33] and Weekers and Roussel [34] have all reported on the use of diisopropyl fluorophosphate (DFP) in the treatment of glaucoma. Agreement continues to be general that it is the strongest miotic agent of its type and that it is the most effective one available in counteracting homatropine and atropine. Its effectiveness as a miotic agent is somewhat neutralized by the discomfort which it causes, due to ciliary spasm. It is of particular value in cases in which surgical measures are

25. Christensen, L., and Swan, K. C.: Adrenergic Blocking Agents in the Treatment of Glaucoma, Tr. Am. Acad. Ophth. **53**:489, 1949.

26. Bloomfield, S., and Haimovici, H.: Effect of Dibenamine® in Chronic Simple Glaucoma, Arch. Ophth. **43**:969 (June) 1950.

27. Ehlers, H.: Diisopropyl Fluorophosphate in Treatment of Glaucoma, Ugesk. f. læger **112**:82, 1950.

28. Gallino, J. A., and Bottini, E. E.: Observaciones clínicas con el empleo de DFP (diisopropil fluorofosfato), Arch. oftal. Buenos Aires **24**:195, 1949.

29. Goedbloed, J.: Quelques faits d'observation avec le di-isopropyl-fluorophosphate, Ann. d'ocul. **182**:885, 1949.

30. Raiford, M. B.: Clinical Evaluation of D.F.P. in Glaucoma Therapy, Am. J. Ophth. **32**:1399, 1949.

31. Stone, W. C.: Use of Di-Isopropyl Fluorophosphate (DFP) in Treatment of Glaucoma, Arch. Ophth. **43**:36 (Jan.) 1950.

32. Vanysek, J.: Di-Isopropyl Fluorofosfat-Nove miotikum, Československ. oft. **5**:8, 1949.

33. Wheeler, J. R.: The Reduction of Intraocular Tension by Curare, Retrobulbar Procaine and Di-Isopropyl Fluorophosphate, Tr. Ophth. Soc. U. Kingdom **69**:209, 1949.

34. Weekers, R., and Roussel, F.: Recherches expérimentales et cliniques sur le mode d'action de l'injection rétrobulbaire d'alcool, Ophthalmologica **118**:115, 1949.

to be avoided at any cost and in cases of secondary glaucoma following cataract extraction. Raiford [20] reemphasized its value in avoiding fluctuation of intraocular pressure as a result of its prolonged effect. He notes that occasionally eyes do become refractory to the drug. Stone [21] also mentions a secondary rise of tension in about 16 per cent of all treated eyes. From reports appearing in the literature, there is no doubt that diisopropyl fluorophosphate is a valuable adjunct in the medical treatment of glaucoma.

Marr and Grob [35] report further observations on the use of tetraethylpyrophosphate in the treatment of glaucoma. This is a substance which acts through inhibition of cholinesterase, somewhat resembling diisopropyl fluorophosphate in its action. It does not, however, inhibit cholinesterase irreversibly, as does diisopropyl fluorophosphate, and its action is considerably shorter. The authors treated 31 eyes with chronic glaucoma, all with the primary wide angle type, except for two with chronic narrow angle glaucoma, one with glaucoma capsulare, one with glaucoma secondary to cataract extraction and one with glaucoma secondary to inactive uveitis. The tension had been uncontrolled in these eyes with pilocarpine, physostigmine and furfuryl trimethylammonium iodide (furmethide®). Tetraethylpyrophosphate was used over a period of five months in concentrations of 0.05, 0.1 and 0.2 per cent in peanut oil, instilled one to three times daily. The tension was maintained below 30 mm. of mercury in only five of the treated eyes. In 20 eyes treatment failed because the tension was not maintained within normal limits, and in 6 eyes use of the drug was stopped because of local symptoms, consisting of severe brow ache, blurred vision and supraorbital pain. In a myopic eye a retinal detachment developed two months after the institution of treatment. The authors' report offers little encouragement for further use of the drug.

Several reports have appeared in the literature on the use of procaine, given either as retrobulbar or as intravenous injections. Although retrobulbar injections of procaine and epinephrine have been used for some time in the treatment of acute congestive glaucoma, further investigation of their mode of action is indicated. Gifford [36] reported extensive studies on the effect of the retrobulbar injection of procaine and epinephrine on the tension of normal and glaucomatous eyes. His observations were based on retrobulbar injections made before 65 operations for cataract and 40 operations for glaucoma. The anterior chamber deepened, and the tension fell about 33 per cent in eyes

35. Marr, W. G., and Grob, D.: Some Ocular Effects of a New Anticholinesterase: Tetraethyl Pyrophosphate (TEPP) and Its Use in the Treatment of Chronic Glaucoma, Am. J. Ophth. **33**:904, 1950.

36. Gifford, H., Jr.: A Study of the Effect of Retrobulbar Anesthesia on the Ocular Tension and the Vitreous Pressure, Am. J. Ophth. **32**:1359, 1949.

having cataracts and from 60 per cent to not at all in eyes with glaucoma. He found that injections of epinephrine solution alone were not as effective as the drug combined with procaine. He pointed out that either drug, used alone, reduced the intraocular pressure. Because epinephrine acts by stimulating the sympathetic nerves, he felt that procaine must lower the intraocular tension by blocking the parasympathetic activity of the third nerve and ciliary ganglion. Fenwick [37] reports that the retrobulbar injection of procaine and epinephrine will temporarily reduce the tension and congestion in about one fourth of all eyes with acute congestive glaucoma, permitting surgical procedures under more favorable circumstances. Esente [38] advocates the slow intravenous injection of 10 to 20 cc. of 2 per cent procaine hydrochloride in the treatment of acute congestive glaucoma. He states that the intraocular pressure begins to decrease about two hours after the injection, reaching its lowest figure about six hours later. He presents 8 cases to substantiate his claims. Givner and Graubard,[39] on the other hand, report no reduction in tension in 10 cases after the intravenous use of procaine. Two patients with absolute glaucoma obtained some relief from pain.

Weekers and Roussel [34] report studies showing that retrobulbar injections of alcohol in rabbits, and to a less extent in man, damage the parasympathetic fibers and ciliary ganglion. This was manifested by sensitization of the sphincter pupillae to acetylbeta-methyl choline and by failure of physostigmine or diisopropyl fluorophosphate to produce miosis. Maumenee [40] emphasized the usefulness of retrobulbar injection of alcohol for relief of pain in absolute glaucoma, a particularly useful procedure in cases of elderly patients in which enucleation must be deferred for some reason. Maumenee also suggests that it be used in less advanced cases of glaucoma in which the disease fails to respond to medical therapy. However, the danger of diplopia, as well as of possible injury to the optic nerve, is a deterrent.

Bloomfield and Kellerman [41] report observations made on 41 eyes having uncontrolled chronic simple glaucoma with residual fields limited to 10 degrees from fixation or less. Of 19 of these eyes, which were treated surgically for reduction of the tension, visual acuity was

37. Fenwick, G. deL.: A Therapeutic Step in Chronic Glaucoma, Brit. J. Ophth. **33**:688, 1949.

38. Esente, I.: Intravenous Use of Procaine in Treatment of Glaucoma, Ophthalmologica **117**:147, 1949.

39. Givner, I., and Graubard, D. J.: The Use of Procaine Intravenously in Ophthalmology, Am. J. Ophth. **32**:1117, 1949.

40. Maumenee, A. E.: Retrobulbar Alcohol Injections: Relief of Ocular Pain in Eyes With and Without Vision, Am. J. Ophth. **32**:1502, 1949.

41. Bloomfield, S., and Kellerman, L.: Therapeutic Results in Advanced Chronic Simple Glaucoma with Telescopic Fields, Am. J. Ophth. **32**:1177, 1949.

subsequently lost in 84 per cent, falling to less than 20/200 in 47 per cent over a follow-up period of two years. On the remaining 22 eyes no operation was performed, although the tension remained uncontrolled under medical treatment. Of this group, over a comparable period, visual loss occurred in only 36 per cent, visual acuity being reduced to less than 20/200 in 14 per cent. The authors feel, therefore, that surgical intervention is contraindicated in eyes with only residual visual fields.

D. Surgical Treatment of Primary Glaucoma.—The literature during the past year reflects increasing interest in various procedures for cautery of the ciliary body. Emphasis has been placed on the probability that tension is lowered through diminution of the blood supply of the ciliary body, with subsequent atrophy. Following such reasoning, Reiser [42] advocates placement of the punctures 8 mm. from the limbus, care being taken to cauterize the insertion of the muscles in order to close off the ciliary arteries. Weekers [43] emphasizes the fact that diathermy produces lowered tension in rabbits even when applied far behind the cilary body. He, however, attributes this to a possible vasodilatation in the area. The fact that the punctures seem effective when applied well back from the limbus is emphasized in papers by Biozzi,[44] Arato [45] and Schreck,[46] who recommend coagulating well posteriorly to catch the long posterior ciliary arteries. Arato [45] placed 10 to 12 punctures immediately in front of the muscle tendons and reported excellent results in cases of chronic simple glaucoma. Most of the reports are enthusiastic as to the value of the procedure.

Berens, Sheppard and Duel [47] reported a technic which employs electrolysis of the ciliary body rather than diathermy. They believe there is less reaction after electrolysis because it causes a chemical decomposition of tissue, which is controlled. They cite the lessened congestion of the ciliary body and eyeball following electrolysis as compared with that following cyclodiathermy. The lower half of the eyeball is treated with 50 to 75 punctures made with a fine conical straight needle applied 1 and 3 mm. back of the limbus, current of 5 milliamperes

42. Reiser, K. A.: Die "Skleraldiathermiepunktur" (SDP): Eine einfache Glaukomoperation, Klin. Monatsbl. Augenh. **115**:491, 1949.

43. Weekers, L.: Mode d'action des opérations antiglaucomateuses, Ophthalmologica **118**:564, 1949.

44. Biozzi, G.: Sulla coagulazione dell'arteria ciliare posteriore lunga, Gior. ital. oftal. **2**:380, 1949.

45. Arato, I.: La angiodiatermia y su applicación en el glaucoma, Arch. Soc. oftal. hispano-am. **9**:746, 1949.

46. Schreck, E.: Cilo-Anolyse und Cilo-Cyclo-Anolyse: Eine neue Glaukomoperation, Arch. f. Ophth. **149**:95, 1949.

47. Berens, C.; Sheppard, L. B., and Duel, A. B., Jr.: Cycloelectrolysis for Glaucoma, Tr. Am. Ophth. Soc. **47**:364, 1949.

being used for five seconds. Electrolysis causes no postoperative rise in intraocular pressure because contraction of the sclera does not occur. Schreck [48] employs electrolysis in a somewhat different way, believing that cyclodiathermy lowers tension through occlusion of the ciliary arteries. He makes an incision 2 mm. behind the insertion of the medial or lateral rectus muscles or both and inserts a cyclodialysis spatula parallel with the limbus, at right angles to the course of the long ciliary arteries. A current of 5 milliamperes is then applied for five seconds to thrombose the ciliary vessels. He also employs a similar operation, in which he combines the aforementioned procedure with cyclodialysis, applying current to the spatula as the cyclodialysis is accomplished. He reports good results in approximately 75 per cent of cases. Bietti [48] also states that electrolysis produces less reaction than diathermy. He also suggests cauterization of the ciliary body with solid carbon dioxide, simply applying it to the conjunctiva overlying the ciliary regions.

Until now, no general agreement has existed as to the value of cyclodiathermy. In the experience of many who have used it, its effect is only temporary, and if applied too close to the limbus it causes marked disorganization of the angle of the anterior chamber, frequently with severe corneal changes. Newer methods of electrolysis, however, may obviate many of these difficulties.

Most of the other papers on surgical treatment of glaucoma appearing during the past year take cognizance of the gonioscopic classification of glaucoma into wide and narrow angle types. Since the operative treatment is largely empirical and mechanical in nature, it would seem that the structural features of the eye should be seriously considered in the choice of surgical procedures. Most of the reports in the literature are in agreement that acute, or narrow angle, glaucoma is best treated, early in its course, by iridectomy, whereas the wide angle, chronic simple, type is best treated by a filtering operation, either internal or external. Most ophthalmic surgeons who follow such concepts believe that iridectomy acts through keeping the angle open and not permitting the iris to come in contact with the trabecular area, whereas filtering procedures provide a new drainage channel for escape of aqueous. Weekers and Duke-Elder, however, feel that operations for primary glaucoma probably exert their effect through changes in the neurovascular system of the eye. Such differences of opinion, however, can be resolved only when more is known about the true nature of the disease.

O'Brien and Weih [49] describe their technic for cyclodialysis, which is somewhat different from the classic procedures of Heine and Blascowics.

48. Bietti, G.: Surgical Intervention on the Ciliary Body: New Trends for the Relief of Glaucoma, J. A. M. A. **142**:889 (March 25) 1950.

49. O'Brien, C. S., and Weih, J.: Cyclodialysis, Arch. Ophth. **42**:606, 1949.

A scleral incision is made only 4 mm. back of the limbus, to diminish the danger of hemorrhage. By making the incision so near the limbus and by not sweeping the spatula posteriorly, the anterior ciliary arteries are avoided, for they perforate the sclera approximately 2 mm. anterior to the insertion of the tendon of each rectus muscle. The cyclodialysis spatula is carried straight forward into the anterior chamber, it is withdrawn slightly, and the ciliary body is separated from the scleral spur by repeated small thrusts. Care is taken not to carry the tip of the instrument into the anterior chamber beyond the point where it is just visible, in order to avoid injury to the corneal endothelium and Descemet's membrane. Miotics are used after operation. The authors state that it is the operation of choice for any type of noncongestive glaucoma and hydrophthalmos and for secondary glaucoma after cataract extraction. Not every one would agree with its use for the first two conditions, but cyclodialysis is at present widely used for the treatment of glaucoma following cataract extraction. Lee and Allen [50] report observations, using the same technic, and emphasize the value of preoperative gonioscopic examination in avoiding dense anterior peripheral synechias and large blood vessels in the angle. Campos [51] describes an interesting variation in technic in which he performs cyclodialysis through a transcorneal approach, a technic recommended by his father in 1939.

The mode of action of cyclodialysis has been attributed to the formation of a permanent cleft between the anterior chamber and the suprachoroidal space, permitting drainage of aqueous in that direction, with absorption by the choroidal circulation. This theory originated in 1932 with Elschnig's microscopic observations on an eye in which the tension had been normalized for 15 years. Barkan [52] reports convincing evidence based on microscopic observations on two eyes in which the tension had been successfully controlled by cyclodialysis for 15 months. Both eyes showed separation of the ciliary body from the scleral spur. In one of these eyes the histologic absence of the canal of Schlemm seemed sufficient evidence to indicate that the operation had not been effective by means of its opening a closed angle. In the same paper, Barkan advocates the use of cyclodialysis in the late stage of narrow angle glaucoma in which extensive adhesions have formed in the angle, a point which would arouse controversy.

The number of articles appearing in the current literature attest that the two most popular external filtering operations now in use are the

50. Lee, O. S., and Allen, J. H.: Cyclodialysis: A Discussion of Techniques, Am. J. Ophth. **32**:1713, 1949.

51. Campos, E.: Ciclodiálise transcorneal, Rev. brasil. oftal. **8**:191, 1950.

52. Barkan, O.: Cyclodialysis: Its Mode of Action; Histologic Observations in a Case of Glaucoma in Which Both Eyes Were Successfully Treated by Cyclodialysis, Arch. Ophth. **43**:793 (May) 1950.

corneoscleral trephination and iridencleisis. In general, the corneoscleral trephination is advocated for the surgical treatment of chronic simple glaucoma with wide angles, whereas iridencleisis may be used for either type of glaucoma. De Arruda [53] lists the major advantages of iridencleisis over other antiglaucomatous operative procedures. The technic is simple and offers less danger, either from immediate or from late complications, than do most procedures. It can be used in treatment of almost any type of glaucoma, and the percentage of cures reported is higher than that with any other surgical procedure. Dellaporta [54] reports seeing within two years 11 cases of late infections following Elliot's corneoscleral trephination and Lagrange's operation, in contrast to an incidence of only 0.27 per cent in a series of 2,175 cases of iridencleisis reported in the literature. Weekers and Weekers,[55] although they do not believe that iridencleisis acts through a filtering mechanism, state that this operation is destined to occupy first place among the antiglaucomatous procedures. They state that if a filtering scar does develop, it is of only secondary importance. They report the operation to be successful in 96 per cent of the eyes with chronic glaucoma, 93 per cent of the eyes with subacute glaucoma, 85 per cent of the eyes with acute glaucoma and 70 per cent of the eyes with secondary glaucoma, using as a criterion of success an ocular tension below 25 mm. of mercury. These authors apparently do not take into consideration possible filtration through a flat scar which does not have a bullous appearance. Purtscher [56] and Wolff [57] describe technics for incarcerating only a small peripheral tongue of iris tissue to preserve a round pupil.

Various types of combined operations have been described in the literature during the past year, in which iridectomy is combined with cyclodialysis, cyclodiathermy, trephination of the cyclodialysis and other procedures, but none has yet received sufficient trial to warrant a detailed discussion.

Two new papers have appeared on the use of implants in the eye to maintain fistulous openings. Bick [58] first carried out experimental studies on the use of tantalum in the anterior chamber of animal eyes and found that it was tolerated well by the cornea, iris, ciliary body and

53. de Arruda, J.: Iridencleisis, Arq. brasil. de oftal. **11**:145, 1948.

54. Dellaporta, A.: Spätinfektion nach Elliottscher Trepanation, Wien. klin. Wchnschr. **61**:512, 1949.

55. Weekers, L., and Weekers, R.: Les fondements physiopathologiques et la technique de l'iridencléisis, Ophthalmologica **117**:303, 1949.

56. Purtscher, E.: Zur Technik der Iridenkleisis antiglaucomatosa, Klin. Monatsbl. Augenh. **115**:402, 1949.

57. Wolff, E.: The Subconjunctival ab Externo Approach in Glaucoma, Brit. J. Ophth. **33**:514, 1949.

58. Bick, M.: Use of Tantalum for Ocular Drainage, Arch. Ophth. **42**:373 (Oct.) 1949.

sclera. He was able to observe endothelium lining the fistulas which formed around tantalum plates inserted into cyclodialysis clefts. Four human eyes with glaucoma were treated with tantalum plates similarly inserted into cyclodialysis tunnels. In the four human eyes, the tension became elevated within two weeks after operation. The plate has remained in place in one eye with absolute glaucoma for a year and a half, even though the tension was not controlled. The method seems to offer little promise of becoming a practical clinical procedure. Bock [59] reported the use of rods made of Jena glass or pyrex.[9] Preliminary experiments showed these to be well tolerated in rabbit eyes for periods of three to five months. In some of the animals endothelium was found to grow along the filtration canal outlined by the glass. Two human eyes were operated on in a similar way, the conjunctival flap being first turned down, as in doing an Elliot trephination, and the sclera then incised 1 to 1.5 mm. back of the limbus, using a narrow keratome or the ab externo route. The scleral incision was made just large enough to allow the end of the glass rod to pass; one end was then placed just within the anterior chamber. Early massage was carried out. It was stated that the effect on the tension was very good in both patients, although specific tension levels were not given. One of the patients had absolute glaucoma and the other advanced chronic congestive glaucoma, for which repeated operative procedures had previously been carried out, without success.

II. CONGENITAL GLAUCOMA

Evidence is beginning to appear in the literature confirming the importance of Barkan's work in reviving goniotomy, modifying its technic and adapting it to the treatment of congenital glaucoma. In his last paper, he reported on the results of operation on 76 eyes for infantile glaucoma, tension being normalized in 66 eyes with maintenance of vision for periods ranging from one to 10 years. During the past year, Callahan,[60] McKinney [61] and Scheie [62] have all added their experiences to the literature. Callahan [60] reported good results in seven of 10 children operated on under the age of 3 years, with a follow-up period of six to 12 months. In the other, older group, with ages ranging from 3½ to 17 years, operation was successful in only 1 of 7 eyes. Callahan agreed

59. Bock, R. H.: Subconjunctival Drainage of the Anterior Chamber by a Glass Seton, Am. J. Ophth. **33**:929, 1950.

60. Callahan, A.: A Frequently Overlooked Cause of Blindness in Infants: Congenital Glaucoma, J. M. A. Alabama **19**:13, 1949.

61. McKinney, J. W.: A Successful Case of Repeated Goniotomy for Congenital Glaucoma, Am. J. Ophth. **33**:132, 1950.

62. Scheie, H. G.: Goniotomy in Treatment of Congenital Glaucoma, Arch. Ophth. **42**:266 (Sept.) 1949.

with Barkan that in the older age group the long-continued pressure obliterates the canal of Schlemm. Early operation therefore was advised. McKinney [61] reports operating on an infant 8 months of age with typical infantile glaucoma. A goniotomy was first done on the right eye and a cyclodialysis on the left. The tension subsequently rose in each eye, and goniotomy was repeated on each side, with control of the tension in each eye. McKinney [62] describes his technic and mentions successful results in five eyes. Scheie [63] reports goniotomies on 16 eyes with infantile glaucoma. The tension was controlled in 11 of these eyes. Failure occurred only in three eyes in which the disease was very advanced and in 2 eyes with glaucoma secondary to Sturge-Weber disease. Emphasis is placed on early diagnosis and prompt surgical treatment, as advocated by Barkan.[64] In all the cases described in this report the patients have been followed three years or longer, with no recurrences. The operations were performed with aid of a goniotomy contact lens.

Weekers and Weekers [65] recommend iridencleisis as the operative procedure of choice for congenital glaucoma. The authors claim that goniotomy is not a desirable procedure because the incision in the angle does not remain open. They also feel that any operative procedure for glaucoma is effective through its action on the ocular neurovascular system and therefore must be carried out on the region of the ciliary body, even in the congenital type. They apparently dismiss the possibility of a mechanical obstruction of the angle as a cause of the disease. Their ideas are in disagreement with workers in this country. Weekers and Weekers [65] suggest the use of cyclodiathermy in far advanced cases. Haik, Breffeilh and Boggess [66] report having treated hydrophthalmos successfully with beta radiation. An Iliff applicator was placed over the ciliary body at 9 and 4 o'clock for 10 minute periods, using 50 mg. of radium screened with 0.1 mm. of monel® metal; a total dose of 50 minutes at 9 o'clock plus 30 minutes at 3 o'clock was used.

III. SECONDARY GLAUCOMA

Secondary glaucoma continually comprises more entities, as the causes of types formerly included in the so-called primary glaucoma group are being identified. The most clearcut explanations appear to be

63. McKinney, J. W.: Goniotomy for Congenital Glaucoma, J. Tennessee M. A. **42**:277, 1949.

64. Barkan, O.: Technique of Goniotomy for Congenital Glaucoma, Arch. Ophth. **41**:65 (Jan.) 1949.

65. Weekers, L., and Weekers, R.: Le traitement du buphthalmos, Ann. d'ocul. **182**:869, 1949.

66. Haik, G. M.; Breffeilh, L. A., and Boggess, J. E.: Treatment of Congenital Glaucoma with Beta Radiation: Report of a Case, New Orleans M. & S. J. **102**:182, 1949.

found in conditions in which obstruction to the trabeculum has occurred for one reason or another. The classic one of these is thought to be glaucoma secondary to exfoliation of the lens capsule, a disease which runs the course of glaucoma simplex. Quite general agreement has existed that the elevated tension is due to obstruction of the trabecular region by exfoliated capsular material and migratory pigment. In cases of unilateral involvement the difference between the angle in the glaucomatous eye and that in the normal eye is striking. Almost invariably the eye with glaucoma shows, in addition to capsular flakes along the pupillary border angle, a very heavily pigmented trabeculum. Thomassen,[67] however, brought forth conflicting evidence when he found that only four of 45 eyes with glaucoma secondary to exfoliation of the lens capsule showed capsular flakes in the chamber angles. He believes, therefore, that the rise in ocular tension did not result from trabecular obstruction. D'Ombrian [68] describes a delayed type of glaucoma following trauma to the eyes. This he believes was due to a lesion in the trabecular meshwork, either fibrosis or a cuticular proliferation similar to that described by Reese. No pathological reports or gonioscopic findings are presented to support this hypothesis.

Glaucoma secondary to obstruction of the entrance to the angle by pushing forward of the iris to make contact with the trabecular area with intumescent lenses following lenticular swelling, is described by Sternberg and Meyer.[69] They report poor results with miotic therapy and advise iridencleisis instead. The lens may be extracted later, with the incision placed either inferior or anterior to the site of the incarceration of the iris. They do not advocate extraction of the lens during the acute attack because they feel that the hazard is too great. Sugar [70] adds still another entity to the secondary glaucoma group when he reports 3 eyes with spontaneous rupture of the lens capsule. He suggests that the glaucoma resulted from one of three possibilities: (1) chemical irritation by lens substance; (2) increased protein content of the aqueous, which tends to lessen the osmotic differential between the aqueous and the blood serum, and (3) obstruction of the trabecular spaces by particles of lens material.

67. Thomassen, T. L.: The So-Called Capsular Glaucoma, Acta. ophth. **27**:423, 1949.

68. D'Ombrian, A.: Traumatic or "Concussion" Chronic Glaucoma, Brit. J. Ophth. **33**:495, 1949.

69. Sternberg, P., and Meyer, S. J.: Choice of Operation in Acute Glaucoma Secondary to Swelling of the Lens, Am. J. Ophth. **33**:763, 1950.

70. Sugar, H. S.: Acute Secondary Glaucoma Due to Spontaneous Rupture of the Lens Capsule, Am. J. Ophth. **32**:1509, 1949.

Gartner and Schlossman [71] review the literature on glaucoma associated with retinitis pigmentosa and report eight cases of their own, seven of congestive glaucoma, and the eighth probably of the same condition. They conclude that the incidence of glaucoma associated with retinitis pigmentosa is somewhat high to be a coincidence, yet not sufficiently high to appear secondary to the retinitis pigmentosa. Pathological and gonioscopic studies revealed no abnormality of the trabecular region. They therefore conclude that glaucoma associated with retinitis pigmentosa is not due to a mechanical block of the angle with pigment, although they feel that it could result from a toxic process which injures the trabeculum, alters its permeability and thus produces glaucoma.

Kalt [72] gives an excellent review of hypertensive uveitis, a disease which presents some of the most difficult situations in ophthalmology. He divides the disease into various categories, ranging from glaucoma associated with primary acute iridocyclitis to gross deformities, such as seclusion of the pupil and obstruction of the angle of drainage. He emphasizes the importance of gonioscopic studies to clarify the state of the angle of the anterior chamber, as well as to study the aqueous humor. The essential pathological characteristic in most cases seemed to be an increase in permeability of the capillaries of the inflamed uvea, which led to intraocular edema, a condition which can adequately be demonstrated by the state of the capillary permeability to intravenously administered fluorescein. This factor, together with difficulties in the drainage mechanism caused by the plasmoid nature of the aqueous humor, was thought possibly to be reenforced, in many instances by mechanical obstruction of the angle of the anterior chamber. A lucid discussion of the treatment of glaucoma associated with uveitis is given. The use of atropine rather than pilocarpine is emphasized. Most ophthalmologists would be in agreement with this premise. The author mentions the therapeutic value of retrobulbar injection of alcohol, which not only relieves pain, but also has a tension-lowering effect, by blocking reflexes which tend to increase vascular stasis in the uveal tract. Surgical treatment, at least in the acute states, should be confined to repeated paracenteses. If permanent drainage is necessary, he advocates iridencleisis. He gives a guarded prognosis, stating that 36 per cent of the affected eyes become blind, the worst prognosis being with sympathetic ophthalmia.

François [73] reports gonioscopic observations on 13 cases of subacute and chronic uveitis during and after the hypertensive phase. Abnormality

71. Gartner, S., and Schlossman, A.: Retinitis Pigmentosa Associated with Glaucoma, Am. J. Ophth. **32**:1337, 1949.

72. Kalt, M.: Les uvéites hypertensives: Étude clinique, pathogénique et thérapeutique, Arch. d'opht. **9**:601, 1949.

73. François, J.: La gonioscopie dans les uvéitis hypertensives, Ophthalmologica **119**:44, 1950.

which he thought might have caused the elevated ocular tension was found in only three of the cases.

Reports on the value of ACTH are just beginning to appear in the literature. Olson [74] and his associates and Gordon and McLean [75] report on the use of this substance. One patient with secondary glaucoma was treated by each group of observers. The tension was reduced in each case, but Gordon and McLean report that it became elevated to its former level within eight hours. The therapeutic value of this substance must await further study.

74. Olson, J. A.; Steffensen, E. H.; Marquis, R. R.; Smith, R. W., and Whitney, E. L.: Effects of ACTH on Certain Inflammatory Diseases of the Eye, J. A. M. A. **142**:1276 (April 22) 1950.

75. Gordon, D. M., and McLean, J. M.: Effects of Pituitary Adrenocorticotrophic Hormone (ACTH) Therapy in Ophthalmologic Conditions, J. A. M. A. **142**:1271 (April 22) 1950.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

The National Interprofessional Committee on Eye Care.—The National Interprofessional Committee on Eye Care, comprised of ophthalmologists, optometrists and opticians representing the various societies in their fields, held its first meeting Oct. 8, 1950, in Chicago, concurrently with the annual meeting of the American Academy of Ophthalmology and Otolaryngology. Officers were elected and agenda drawn up for discussion by the committee.

Dr. Avery D. Prangen, ophthalmologist, Mayo Clinic, Rochester, Minn., was chosen chairman for the coming year, and Mr. Leslie Myers, Minneapolis, vice chairman. Dr. Carel C. Koch, editor, *American Journal of Optometry* and secretary of the American Academy of Optometry, was elected secretary. Other members of the committee are Mr. Henry B. Carpenter, guild optician, Syracuse, N. Y.; Dr. Frederick C. Cordes, professor of ophthalmology, University of California Medical School, San Francisco; Dr. Arthur M. Culler, professor of ophthalmology, Ohio State University, Columbus, Ohio; Dr. H. Ward Ewalt Jr., optometrist, Pittsburgh; Dr. Franklin M. Foote, executive director, National Society for the Prevention of Blindness, New York; Dr. Henry A. Imus, physicist, Office of Naval Research, Washington, D. C.; Mr. Norman A. MacLeod, wholesale optician, Providence, R. I., and Dr. Glenn H. Moore, optometrist, Chicago. Dr. William F. Hughes Jr., professor of ophthalmology, University of Illinois School of Medicine, Chicago, will also serve on the committee as alternate.

Problems discussed at this first session included, besides organization, interprofessional relationships and various other topics related to improving the optical eye care offered the public by the several groups represented by the committee. In general, the public health aspects of optical eye care were stressed.

The second meeting of the National Interprofessional Committee on Eye Care is scheduled for December 17, in Chicago, and will be held concurrently with the annual meeting of the American Academy of Optometry.

Course in Ocular Pathology, Tulane University of Louisiana School of Medicine.—The Tulane University of Louisiana School of Medicine announces a course in ocular pathology devoted to a study of tumors of the eye, adnexa and orbit, to be given Feb. 12 through 17, 1951. The fee for the course, which will be limited to an enrolment of 12, is $100. Assisting the regular staff will be Dr. C. S. O'Brien, Dr. John McGavic and Dr. Theodore Sanders. Further information may be obtained by writing to Dr. James H. Allen, Department of Ophthalmology, 1430 Tulane Avenue, New Orleans.

From Feb. 19 through 24, 1951, a symposium on ocular pharmacology and therapeutics will be held at the Tulane University of Louisiana School of Medicine. Limited to 150 registrants, the fee for the course will be $100. Drs. Alson E. Braley, Parker Heath, Irving H. Leopold, P. Robb McDonald, Frank W. Newell and Alan C. Woods will assist the regular staff in conducting the symposium. For further information, write to Dr. James H. Allen, 1430 Tulane Avenue, New Orleans.

Annual Spring Graduate Course, Gill Memorial Eye, Ear and Throat Hospital.—The Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Va., announces to physicians its twenty-fourth annual spring graduate course in ophthalmology, otorhinolaryngology, faciomaxillary surgery, bronchoscopy and esophagoscopy, to be given April 2 to 7, 1951.

For further information write Superintendent, Box 2467, Roanoke, Va.

Annual Clinical Conference, Wills Hospital.—The third annual clinical conference of Wills Hospital, Philadelphia, will be held at the hospital March 16 and 17, 1951. As in other years, papers which reveal the latest developments in ophthalmologic treatment and procedures will be presented by many of the nation's outstanding ophthalmologists.

CORRECTION

In the article by V. Everett Kinsey, Ph.D., entitled "A Modified Concept of Aqueous Humor Dynamics and the Maintenance of Intraocular Pressure," which was published in the August 1950 issue of the ARCHIVES, page 215, the legend for figure 4 should read:

"Movement of different classes of substances from blood and out of the eye. Red arrows refer to water; green arrows, to nonelectrolytes, and blue arrows, to electrolytes, including bicarbonate." (It was originally intended to illustrate the movement of bicarbonate separately, as indicated in the text. For purposes of economy the present plate was substituted.)

SPECIAL NOTICE

For the general information of indexers, catalogers and library personnel with reference to the listing of the new title of this journal, we advise that the *Quarterly Cumulative Index Medicus* policy be followed. The *Quarterly Cumulative Index Medicus* with its volume 49 (January-June 1951) will list this journal under the new title, so that the letters A. M. A. will be included as an integral part of the title. For the completion of volume 48 (July-December 1950) the *Quarterly Cumulative Index Medicus* will continue to use the old title, without adding the designation A. M. A.

Book Reviews

Surgery of Cataract. By Daniel B. Kirby, M.D., LL.D. Price, $30. Pp. 695, with 339 illustrations, including 52 subjects in 21 color plates. J. P. Lippincott Company, 227-231 S. 6th St., Philadelphia, 1950.

The completeness with which every phase of the subject is discussed makes this volume a real monograph. It contains much valuable information because it records not only the wide experience of the author but also the opinions of many others. It is safe to predict that this work will serve for years to come as an integral part of most ophthalmological libraries.

The book is divided into five parts, with the following titles: (1) The Development of Cataract Surgery; (2) Preparation for Cataract Surgery; (3) Present-Day Cataract Surgery; (4) The Correction of Aphakia; (5) Results Obtained in Cataract Surgery. Each of these subjects is meticulously portrayed, with the aid of liberal quotations and numerous excellent illustrations.

Although the chapters on the early history and development of cataract surgery consist largely of quotations from earlier writers, they do form an interesting introduction. Under the title of "Basic Sciences Applied to Cataract Surgery," the embryology, anatomy, physiology and pathology of the lens are presented in a most comprehensive manner. The "Drama of Cataract Surgery" is next unfolded in a wordy exposé. The unique manner in which the author gives the usual instructions on lighting, the care of instruments and the correct behavior of the surgeon and assistant is most striking. He compares the surgical removal of a lens to a theatrical production, in which the final result depends to such a large extent on the smooth function of each component part.

With the aid of many illustrations, the changes that take place in the development of cataract are clearly depicted. The author enumerates the following five standards by which one can judge the progress of cataract: (1) the test of vision, (2) the test with the ophthalmoscope, (3) the test of refraction, (4) the test with the slit lamp microscope, (5) the test of photography.

In the discussion on the medical treatment of cataract the author correctly states "We do not have an adequate program for the nonsurgical treatment of cataract."

Congenital development defects of the lens are beautifully shown, and his views on the timing of the operation for congenital cataract are given. The management of unilateral congenital cataract is dispensed with in these words: "If the fellow eye is normal, or almost so, usually it is best judgment not to interfere with the cataract." The various types of acquired cataract are fully described, and the indications and contraindications for operation clearly given. Although in general the author favors early removal by the intra-

capsular method, he rightly states that no rule can be set because "judgment will be necessary to decide on this point." The diagnosis and treatment of complicated cataract justly receive special consideration and, which is fairly complete except that the author devotes less than one page to glaucoma and cataract, reserving most of his discussion to glaucoma as a postoperative complication. A description of the preoperative preparation of the patient and the various types of surgical procedures used in the treatment of cataract are presented. After noting the salient features of operations for soft cataract and the extracapsular extraction, the author, in a detailed discussion of the methods of intracapsular extraction, first presents many of the technics that are found in the literature and then gives an exhaustive description of his own system of intracapsular cataract extraction. The various types of sutures are similarly described and the reasons stated for his preference of three radially placed postincisional sutures. The author's large experience enables him to speak authoritatively on the prevention and treatment of complications, and his remarks on the loss of vitreous are especially pertinent.

This volume, of almost 700 pages, devoted exclusively to the surgery of cataract, is complete in every detail. Its format is excellent, and the illustrations are numerous and well reproduced; but it was confusing to this reviewer to have some drawings made "from the surgeon's viewpoint" and others in the usual manner. The text is somewhat disconnected and often too verbose; but in spite of these minor objections the book is a valuable addition to ophthalmologic literature. It portrays the ideas of an experienced surgeon and gives the reader full information on the thoughts of others.

Some Relation Between Vision and Audition. By J. Donald Harris. Publication 71, American Lecture Series. Price, $1.50. Pp. 65. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

In this interesting monograph, the author compares the physiology of the eye and the ear. Although there are more differences than similarities, the many correspondences which exist illustrate how these two organs have developed for maximum biologic efficiency.

In comparing the sensitivity of the two organs, the author calls attention to the fact that in terms of energy at threshold in spectral regions where the organs are most efficient the eye and the ear are roughly similar. For vision, 2.2 to 5.7 $\times$ 10^{-10} ergs per second are needed. For audition, about 1 $\times$ 10^{-9} ergs per second are required. With respect to the range of intensities, the eye responds to from 1/10,000 to 1,000,000,000 international candles per square meter, and the ear, to from 1/10,000 to 10,000,000 or more dynes per square centimeter. The Weber law, while apparently holding for some ranges of intensity in vision, does not seem to have any value in audition. In the field of single nerve fiber activity, both the optic and the auditory nerve obey all the laws of single nerve fibers. Their rates for conduction of impulses vary with intensity and duration for short durations; after an initial rate, equilibration sets in, and increase in the intensity shortens the period of latency. Other similarities are noted.

This is an extremely interesting lecture for those with some familiarity with visual physiology. It serves to call attention to the fact that, although this volume was published in the series of "American Lectures in Otolaryngology," a similar series, under the direction of Dr. Donald Lyle, is being contemplated for ophthalmology. These publications should serve a very useful purpose, as monographs which are too long for our journals and yet too short for book form.

Recent Advances in Ocular Prosthesis. By J. H. Prince, F.B.O.A., F.S.M.C. Price, $4. Pp. 155, with 89 illustrations. Williams & Wilkins Company, Mount Royal & Guilford Aves., Baltimore 2, 1950.

This is a companion volume to "Ocular Prosthesis." It is a small book, of 155 pages, dealing exclusively with the recent technic for orbital implants. It is concisely written, well illustrated, and should be available to all who are interested in ophthalmic surgery.

Surgery of the Eye: Injuries. By Alston Callahan, B.A., M.S. (Ophth.), M.D., F.A.C.S. Price, $11.50. Pp. 217, with 357 illustrations, including colored plates. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This monograph is a concise presentation of the modern surgery of ocular injuries. It is concerned not so much with the history and development of plastic surgery as it is with clearcut, useful descriptions of those technics of repair which have been found successful in recent years. The first part of the book deals with traumatic lesions of the globe in such a brief fashion that it is little more than an outline. The second, more detailed section covers both primary and secondary repair of lacerations and deformities in and about the orbit. Here more than one surgical technic is often presented for the treatment of a given injury. These technics are those which should be a part of the armamentarium of any ophthalmic surgeon interested in plastic repair. In these descriptions the author is aided by a series of drawings and photographs, many of which are excellent. There are, of course, some surgical procedures with which one does not entirely agree, such as, for instance, the use of fascia lata implants to repair deformities of the upper lid after an enucleation of the globe. There are also technics which, in other hands, have been unsuccessful. One of these is the repair of a large coloboma of the upper lid without employing a canthotomy. Similarly, it may be felt by some that too much emphasis is placed on the repair of the gross orbital deformities so often seen in wartime, at the expense of the less extensive ones that occur more frequently in civilian life.

This is not a theoretical treatise; it is a factual book supplied with an adequate bibliography. The author is to be commended on the clarity and conciseness of his writing, and the book will serve as a valuable and practical addition to the library of the ophthalmic surgeon. In it one can find the surgical repair of most traumatic lesions dealt with in an intelligent manner, with ample illustrations to portray clearly the technic employed.

Worth's Squint. By T. Keith Lyle. The Binocular Reflexes and the Treatment of Strabismus. Pp. 319, with 182 illustrations. The Blakiston Company, 1012 Walnut St., Philadelphia 5.

This is in reality the eighth edition of Worth's "Squint," which has recently appeared under the pen of T. Keith Lyle. No one has had as much influence on the philosophy of squint since Worth's passing as Bernard Chavasse. Chavasse was the first to seize on the work of Sherrington, Magnus and Pavlov and to interpret squint as a perversion of the binocular reflexes. He was the first to place the etiology, diagnosis and treatment of strabismus on a sound psychological basis; and yet his book, for all its excellence of prose, required such careful reading and rereading that it was appreciated only by a relative few who were willing to give it the time it deserved.

Lyle has undertaken a difficult job and done it well. He has condensed the first edition and sought to clarify wherever possible some of the concepts of reflex development so as to make the ideas intelligible to those with little experience in this field of physiology. In doing so, he has frequently lost some of the beauty of Chavasse's style, which in many places was rather poetic. It seems a shame, to pick out but one example, to lose such paragraphs as the following:

"What are these reflexes? On what primitive foundations, almost elemental in their age and unconditional stability, are they based? What new, and at first unstable, reflexes grew out of these ancient and more stable ones? See, in tentative and yet surviving succession, the slow unfolding of reaction after reaction, reflex upon reflex, the ascending series, until, in humble splendor, there stands at last revealed the fulness of the stature of the binocular machine. It is a romantic story."

In many places, Lyle has added considerably to the value of the book, especially in the methods of diagnosis and treatment. He has wisely left out those operations included by Chavasse, which he, Lyle, does not use and which, like thermoplasty, were probably used by few other ophthalmic surgeons than Chavasse himself. This revision will undoubtedly retain the leadership in this field which the first edition obtained with very little competition.

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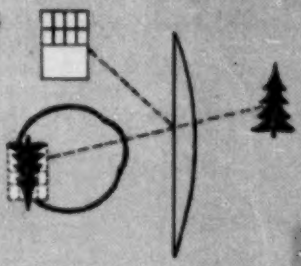

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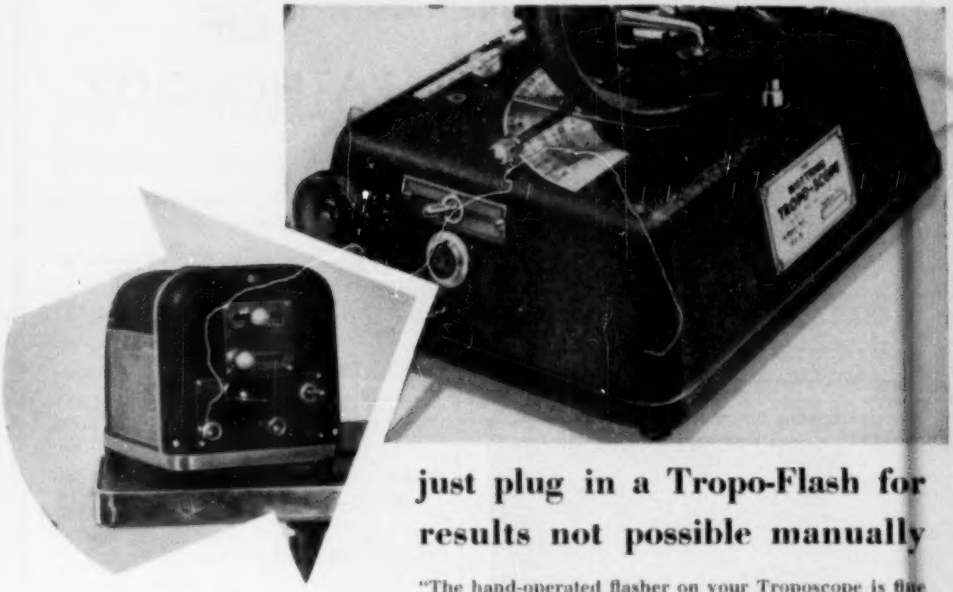

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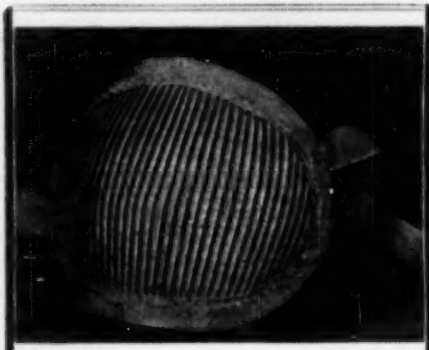

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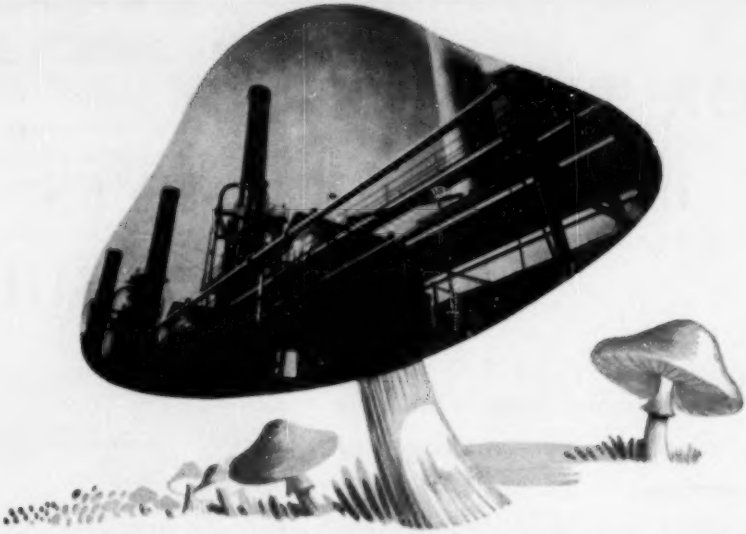

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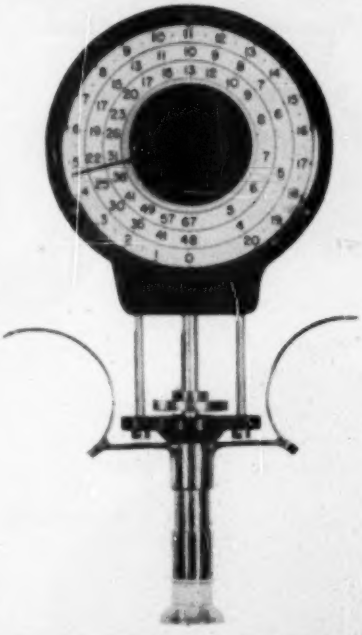

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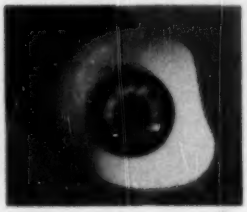

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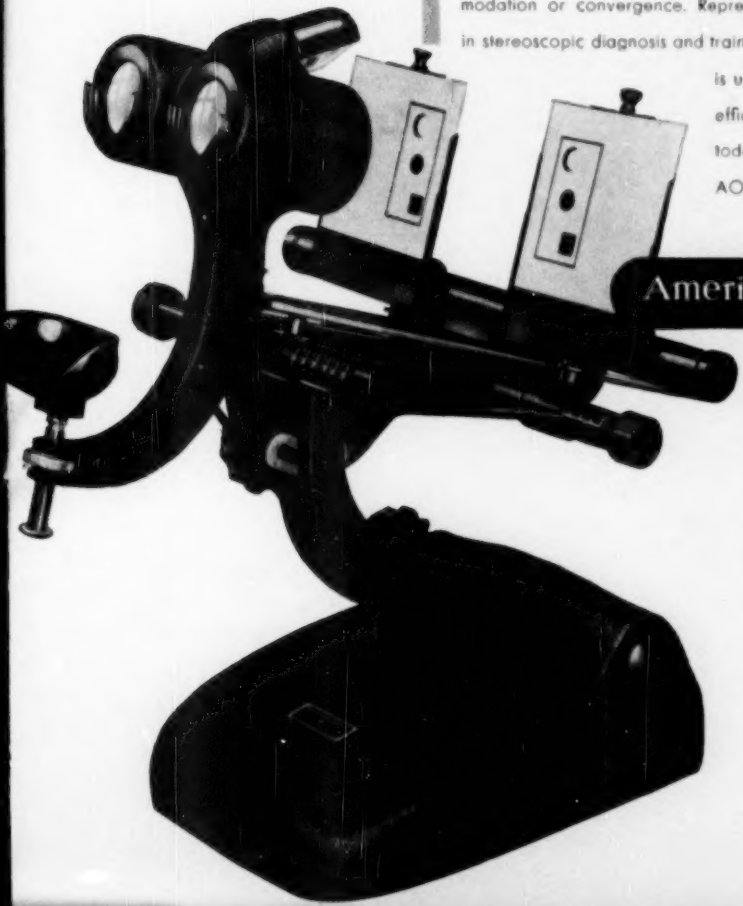

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